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A STUDY OF SODIUM AND WATER BALANCES IN CONGESTIVE CARDIAC FAILURE.[1]

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A COMMON TYPE of cardiac failure is that which is associated with venous congestion and fluid retention. The clinical features of this aspect of cardiac failure are increased venous pressure, manifested by distension of the veins in the neck and enlargement of the liver, and excess fluid in the body, shown by œdema and effusion into the serous sacs.

At various times different hypotheses have been put forward to account for this disturbance of the circulation. The traditional explanation formulated by Corvisart (1812) and supported by Hope and later by Starling is the "back pressure theory". Physical analysis of this theory shows that weakening of the right side of the heart should cause accumulation of blood in the venous circulation and diminution of the cardiac output, with falling arterial blood pressure. Recent measurements of cardiac output in these patients reveal that left ventricular output is not always reduced and certainly they usually have a normal arterial blood pressure. Further, physical considerations of the circulatory system indicate that to get a rise in venous pressure without a fall in arterial pressure in the circulation implies that the "static" pressure in the vascular system—as opposed to the dynamic pressures commonly measured—must be raised. This means that after death, when the blood flow has ceased, the pressure (static) in the system must be above normal. Starr (1940) demonstrated in a series of cases in which death occurred during congestive cardiac failure that the "static" venous pressure averaged 20·3 centimetres of water, in contrast to the normal value of 7·6 centimetres of water.

To obtain an increase in the "static" pressure of the system it is necessary either to increase the volume of fluid within it (blood volume) or to decrease its capacity (general vasoconstriction). There is considerable evidence that both these mechanisms function in the production of the congestion of cardiac failure (Warren and Stead, 1944; Reichsman and Grant, 1946; McMichael, 1946).

It appears, therefore, that the cause of the congestion must be sought outside the heart, although without doubt the train of events frequently is started by cardiac damage.

Associated with the increase in blood volume is an increase in the extracellular fluid volume of the body, often gross enough to produce pitting œdema. Analysis of this œdema fluid shows that it has a sodium content very similar to that of normal plasma. This means that in addition to fluid retention within the body there must be sodium retention. As the only important route of sodium excretion from the body is in the urine, this retention implies either diminished filtration of sodium through the renal glomeruli or excessive reabsorption from the renal tubules. In this connexion it must be remembered that the excretion of both water and sodium by the kidney is to some extent under hormonal control by the posterior pituitary lobe and adrenal glands.

The following diagram, adapted from Starr (1949), gives a possible train of events leading to the congestion of cardiac failure.

In this paper evidence is submitted that there are two types of congestive cardiac failure which differ in their response to treatment.

[1] Read at a meeting of the Section of Medicine, Australasian Medical Congress (British Medical Association), Seventh Session, Brisbane, May-June, 1950.

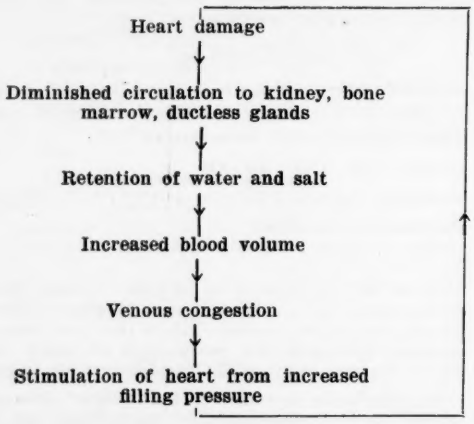
Observations.

The observations here recorded cover four cases of congestive cardiac failure, which were clinically similar save for the type of the underlying cardiac disease, and were representative of many others studied.

The patients at first were confined to bed and given a diet with a known content of sodium, which was restricted below the normal intake in varying degrees. They were encouraged to drink freely of sodium-free fluids. Digitalis preparations were exhibited only to those patients who had been taking them prior to admission to hospital, in which case they were continued in the previous dosage. If there was no reduction in the congestion after a period of some two to three weeks, mercurial diuretics were exhibited.

A free fluid intake, whilst the sodium intake was restricted, was advised because there is an upper limit to the sodium concentration in urine, and so the greater the urine flow per day, the greater the possible excretion of sodium. If, at the same time, the intake of sodium is restricted a negative balance may be set up, and concomitantly fluid is lost from the body.

The fluid intake and urine output were measured and allowances made for the unmeasured fluid gain from metabolism and fluid loss from the lungs, skin and fæces.



Similarly, the sodium intake and output in the urine were measured, but no allowance was made for the small sodium losses in the fæces and sweat.

CASE I.—E.M., a woman, aged sixty-four years, was admitted to hospital on August 7, 1949, in a state of congestive cardiac failure associated with mitral stenosis and auricular fibrillation. She had suffered from attacks of rheumatic fever at the ages of nine and twelve years. Auricular fibrillation had commenced eight years before her admission to hospital. Attacks of congestive cardiac failure had occurred two years and one year before admission. For three months prior to admission she was becoming progressively more dyspnœic, and generalized œdema had developed. Examination on admission showed gross œdema of the lower limbs and lower part of the trunk, and considerable ascites. When the patient was sitting upright the neck veins were distended for nine centimetres above the clavicle. Her liver was considerably enlarged. Treatment followed the regimen set out, and fluid intake amounted to some 1600 millilitres per day. As she had been taking a digitalis preparation prior to admission, this was continued ("Digoxin" 0·25 milligramme every eight hours). On the eighth day of treatment her sodium intake was restricted to approximately 220 milligrammes of sodium (ions) per day. By the thirty-fourth day of treatment she was completely free from œdema and was moving freely about the hospital.

Figure I shows her progressive body weight and her daily water and sodium balances. During the period of treatment she lost 12 kilograms in weight. The points illustrated by this chart are three. First, although there was a gain in weight over the first four days, fluid (solid line) was retained at a diminishing rate until on the fifth day she was in a state of fluid balance; after this an increasing fluid loss developed until the twenty-sixth day, after which the loss diminished daily to reach again a balanced state on the thirtieth day. Secondly, from the fifth to the thirty-fifth day she was losing sodium in amounts which corresponded quantitatively with the water loss, if it is assumed that sodium and water are lost in the same ratio as they occur in the œdema fluid (approximately 3300 milligrammes of sodium (ions) per litre of water). Thirdly, the water balance curve indicates that from the onset of treatment in bed the patient's water metabolism was being corrected and was little influenced by the severe restriction of sodium intake.

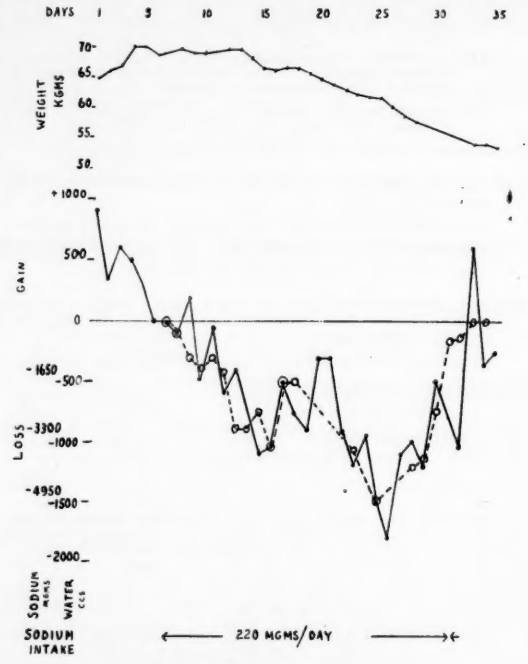


FIGURE I.

Case I. Graphs showing the daily weight (above) and the daily water (solid line) and sodium (broken line) balances (below).

CASE II.—P.C.B., a woman, aged seventy-one years, was admitted to hospital on October 29, 1949, in a state of congestive cardiac failure associated with atherosclerosis, hypertension, auricular fibrillation and aortic regurgitation. For ten years she had had pronounced exophthalmos, but there was no evidence of thyreotoxicosis. For the past year she had been under medical treatment, and intermittent auricular fibrillation is recorded in her history. For one month prior to admission she had noticed severe swelling of her legs and much shortness of breath, even in bed. Examination at the time of admission showed an orthopnœic patient with extensive œdema of the lower limbs and an effusion in the right side of her chest. Her arterial blood pressure was 210 millimetres of mercury (systolic), 60 millimetres (diastolic), and her neck veins were distended. In the treatment of this patient the sodium intake was restricted to one gramme of sodium (ions) per day, and her fluid intake was of the order of 1300 millilitres per day. By the eighteenth day of treatment the patient was free from œdema and was freely moving about the hospital. No digitalis preparation was exhibited during treatment, and although auricular fibrillation was still present at the end of the period of observation, the ventricular rate was 76 beats per minute.

Figure II shows the progressive body weight and water and sodium balances daily. During treatment her body weight fell by 11 kilograms. These curves illustrate the

same points as those of Case I, namely, the initial rise in weight, the change in water metabolism from the beginning of bed rest, and the close correlation between water and sodium losses.

An assay of the patient's urinary excretion of pituitary antidiuretic hormone was made towards the end of the period of observation and it was found to be within normal limits.

CASE III.—H.R., a man, aged eighty-eight years, was admitted to hospital on January 24, 1950, in a state of congestive cardiac failure associated with senile myocardial degeneration. For two weeks prior to admission he had

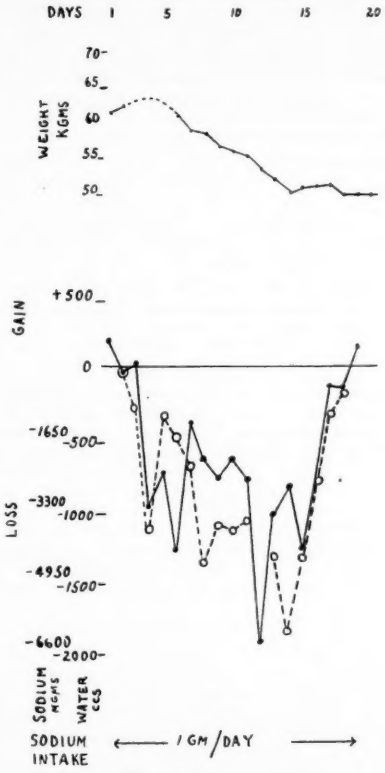


FIGURE II.

Case II. Graphs showing the daily weight (above) and the daily water (solid line) and sodium (broken line) balances (below). A.D.H. = pituitary antidiuretic hormone.

become progressively more dyspnœic and had developed increasing œdema of his legs. Examination on admission showed extensive œdema of his lower limbs and the lower part of his trunk. There was evidence of pulmonary congestion, effusion into the right pleural cavity, an enlarged liver and some ascites. Cardiac examination revealed a heart within normal limits except for frequent extrasystoles. He was treated in the routine manner and his fluid intake was of the order of 1600 millilitres per day. His sodium intake was variable, but approximated to one gramme of sodium (ions) per day. After fifteen days on this regimen his weight had slightly increased and there was no evidence of fluid or sodium loss commencing (see Figure III). On the sixteenth day he was given an injection intramuscularly of two millilitres of "Mersalyl", and this was repeated daily for four days. By this time he had lost six kilograms in weight, was œdema-free, and had no evidence of congestion. His cardiac condition then seemed good, but on the twenty-fourth day he rapidly developed circulatory failure and died. An assay of the patient's urinary excretion of pituitary antidiuretic hormone was made on the fifteenth day and showed a great increase above normal.

It is to be noted in this case that the sodium and water retention or loss follow closely one another, but that, unlike Cases I and II, no diuresis was produced by the treatment in this case until mercurial diuretics were exhibited.

CASE IV.—M.N., a man, aged forty-two years, was admitted to hospital on July 19, 1949, in a state of congestive cardiac failure associated with arterial hypertension. He was known to have had hypertension for seven years, but only in the past seven months had he been conscious of dyspnœa on

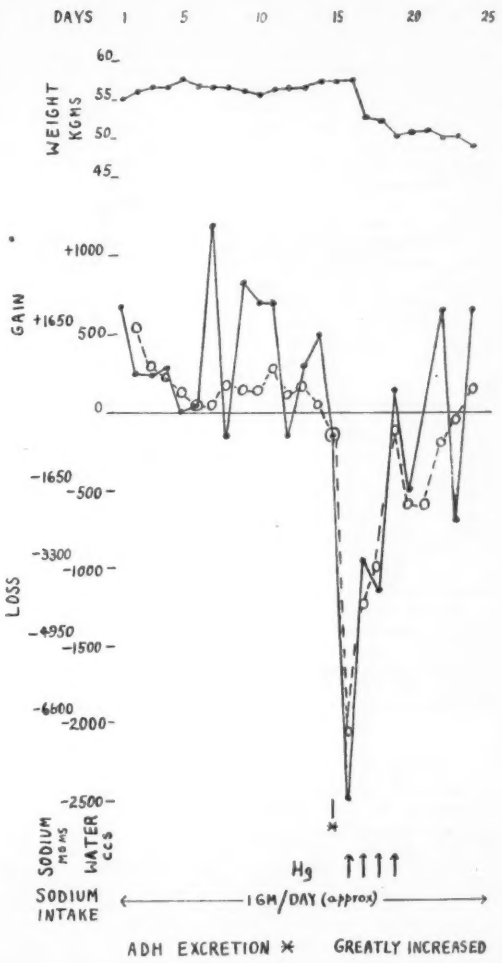


FIGURE III.

Case III. Graphs showing the daily weight (above) and the daily water (solid line) and sodium (broken line) balances (below). Mercurial diuretics administered on days marked with a vertical arrow. A.D.H. = pituitary antidiuretic hormone estimated on day marked with an asterisk.

exertion. For three weeks he had noticed dyspnœa on slight exertion and during this period had developed œdema of his legs. Examination on admission showed an orthopnœic man with an arterial blood pressure of 195 millimetres of mercury (systolic), 148 millimetres (diastolic) There were moist sounds throughout his lungs, and his liver was moderately enlarged. In the treatment of this patient the fluid intake was of the order of 2000 millilitres per day, and his sodium intake was restricted to 220 milligrammes of sodium (ions) per day. He was kept on this regimen for fifteen days, during which time his weight fell by four kilograms, but he did not become free from œdema. His diet was then increased and contained one gramme of sodium (ions) per day. After this his weight and congestive state gradually increased. On

the twenty-ninth and thirty-fourth days of treatment he was given injections of a mercurial diuretic, which produced a large diuresis and a loss of seven kilograms in weight. He was then œdema-free and moving around freely. Throughout the period of observation his blood pressure did not alter significantly.

The chart (Figure IV) of his progressive weight and daily water and sodium balances shows great differences from those in the first two cases and some similarities to that in Case III.

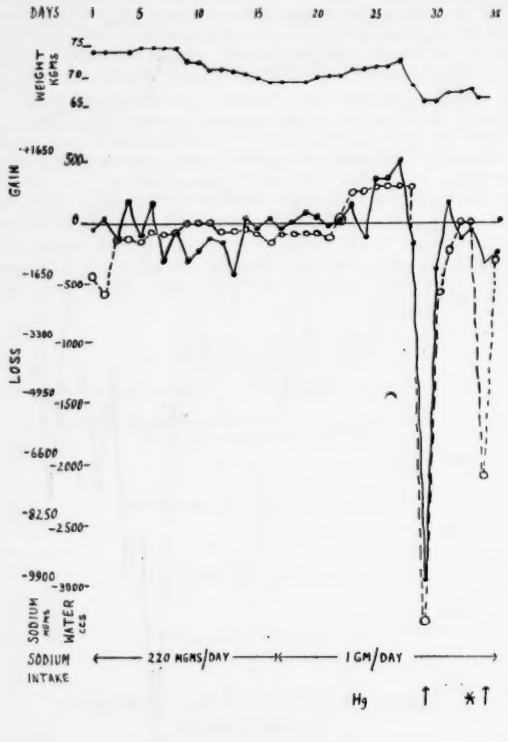


FIGURE IV.

Case IV. Graphs showing the daily weight (above) and the daily water (solid line) and sodium (broken line) balances (below). Mercurial diuretics administered on days marked with a vertical arrow. A.D.H. = pituitary antidiuretic hormone estimated on day marked with an asterisk.

Severe restriction of his salt intake, bed rest and free fluids were associated with some loss of œdema fluid, but increase of salt intake increased his œdema. As in Case III, there was a dramatic diuresis following the injection of a mercury diuretic. His urine contained an excess of pituitary antidiuretic hormone when tested on the thirty-third day. However, after an injection of mercurial diuretic on the thirty-fourth day the excretion of antidiuretic hormone was within normal limits. It is to be noted that prior to mercurial diuresis the water and sodium balances do not run parallel, but tend to move in opposite directions.

Discussion.

Consideration of the response to treatment of these four patients shows clearly that the patients in Cases I and II behaved in a different manner from those in Cases III and IV. The first two patients became œdema-free and lost the congestive aspects of cardiac failure after bed rest, restriction of sodium intake and the free ingestion of fluids, but the last two patients failed to respond appreciably to these therapeutic measures. They did, however, respond to mercurial diuretics.

In the quest for the underlying cause of the different responses shown, a clue is possibly given by the high excretion of antidiuretic hormone in those cases in which mercurial diuretics were required. Apparently mercurial diuretics can neutralize the excessive hormone action.

As yet sufficient cases have not been studied to allow the reaching of definite conclusions as to the role of the pituitary gland in congestive cardiac failure, but these cases support Starr's contention that the pituitary gland secretions do play some part in some cases in the production of congestive cardiac failure.

Summary.

1. Congestive cardiac failure has been studied by recording water and sodium balances during treatment of patients on a regimen consisting of bed rest, restriction of sodium intake, free fluid intake and in some cases the exhibition of mercurial diuretics.

2. Four illustrative cases are recorded in detail.

3. The studies reveal two types of subjects of congestive cardiac failure: first, those that respond to bed rest, restriction of sodium intake and the taking of free fluids; secondly, those that fail to respond to this therapy until mercurial diuretics are exhibited.

4. It has been noted that the patients in the second group excreted excess amounts of pituitary antidiuretic hormone in their urine.

Acknowledgements.

I am indebted to Dr. P. Fantl (Baker Institute) for the method of estimating urinary sodium content, to Dr. J. Bornstein (Baker Institute) for the hormone assays, and to the staff of the unit for assistance in many different ways.

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Addendum.

Estimation of Urinary Sodium Content.

The sodium content of urine was measured in the following way. Protein and phosphates were removed from the urine by precipitation with uranium acetate and filtration. From the filtrate sodium zinc uranyl acetate was precipitated and estimated alkalimetrically. From this estimation the sodium content was calculated, appropriate standard solutions being used.

Assay of Antidiuretic Substance in Urine.

The antidiuretic substance was extracted from a twenty-four hour specimen of urine by the technique of Grollman and Woods. This extract was then assayed in rats by Ralli's technique.

This method gives the following "half excretion" times: control animals, 90-110 minutes; urine from normal patients, 110-140 minutes; urine containing excess of antidiuretic substance, more than 160 minutes.

Errata.

In Figure II the number 2000 water ccs. should read 2200; in Figure IV the number 3000 water ccs. should read 3300.

CANCER MORTALITY IN AUSTRALIA.[1]

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IT is difficult to discuss the cancer mortality of individual organs adequately without the background of a systematic review of the total cancer mortality. I propose, therefore, to summarize the Australian official statistics bearing on cancer, in a first paper discussing mortality from all forms of cancer, and then in subsequent papers breaking down the total cancer mortality into the mortality from cancer of the various organs and systems. In the case of some of the individual organs I shall use the information on parity and conjugal state available from official sources.

Definition of the Term "Cancer".

The diseases falling into the categories or "rubrics" of the cancers of the International List are detailed in a coding manual of the Registrar-General of England and Wales (1940), which was based on the Fifth Decennial Revision of the International Commission, Paris, 1938. This note makes the following statement:

> In these groups the term "cancer" includes the following, which are assigned to the part of the body affected: carcinoma; sarcoma; malignant growth, tumour or disease; astrocytoma, blastocytoma, blastoma (with or without prefix), chloroma, chordoma, endothelioma, ependymoma, epithelioma, Ewing's tumour, glioma unless stated to be benign, malignant cachexia, malignant reticulosis, melanoma, myeloma, *papilloma choroideum*, pinealoma, reticular endotheliosis, rodent ulcer, scirrhus, seminoma.
>
> Cancer of the liver, unless stated to be primary, should be regarded as secondary, and also cancer or carcinoma, but not sarcoma, of lymphatic glands.

"Cancer" is thus intended to be read in the general sense of "malignant growth" and not in the limited sense of "carcinoma". Thus the term "cancer" of the official statistics includes "sarcoma" and is practically equivalent to malignant growth of any kind, but includes neither the leuchæmias nor Hodgkin's disease.

Sources of Data.

In *Demography*, the annual bulletin of the Bureau of Census and Statistics, Canberra, tables are given of the deaths from all causes and by each individual cause of the International List of Causes of Death for each sex in five-yearly age-groups. Over the period from 1908 to 1945, that I have chosen for study, there have been changes in the International List, but it will be found that they do not greatly affect the actual assignments of deaths to cancer. Up to 1921, cancers were included in Class I of the International List—that is, in the class of general diseases. For the years 1922 to 1930, the cancers are included in Class II, which then comprised general diseases not included in Class I; Class I had then become the class of the general diseases of known infective origin. However, Class II at this time included also such general diseases as "pink disease" and diabetes. In the years 1931 to 1945 the cancers have been included with "other tumours" in a special class, Class II.

However, besides these tables of the deaths classified according to the principle of the International List, there are supplementary tables, which give the occupation of the decedents from cancer and the type of cancer, and a very much more detailed break-down by site than is possible in the main table; the main table, as we have seen, gives the deaths in the appropriate rubric of the International List. In these detailed lists the age groups up to the age of fifteen years have been consolidated, and I have followed this example in the tabulations of the cancers, since cancer at these low ages has a comparatively low incidence and small numerical importance. Sometimes in discussing the individual cancers I shall consolidate all the age groups up to the age of twenty-five years. For the other age groups I have used a ten-yearly age grouping up to the age of seventy-five years and then combined the age groups above seventy-five years into a single group. This ten-yearly age grouping has been found to reduce the amount of arithmetic without seriously affecting the accuracy of the comparisons to be made between different populations.

The Measurement of the Cancer Mortality.

The Necessity for Using Age-Specific Death Rates.

In order to measure the trend of the cancer mortality I have divided the period from 1908 to 1945 into three decennial periods for the years 1911 to 1940 and the two periods 1908 to 1910, 1941 to 1945. During this time, 1908 to 1945, there have been considerable changes in the age-distribution of the Australian population, such as would render any comparison of mortality by means of the crude (that is, unstandardized) rates of small scientific value. I have relied, therefore, chiefly on the age-specific rates for the two sexes in the studies of the trends of cancer mortality over the years. But this gives us a set of eight rates for each sex for every comparison between different populations or the same population at different times, so that I have followed the custom of giving the standardized rates.

Standardization onto an Actual Population.

This process of standardization may be regarded from two points of view—firstly, as a method of removing the disturbing effect of differences in the age distribution in the populations compared, and secondly, as a method of obtaining a weighted mean or summary of all the age-specific and sex-specific rates. I have used two standard populations, the population of England and Wales, as recorded at the Census of 1901, and a life table population that has been computed from the data of the life tables of

[1] This paper is published with the permission of the Director-General of Health, Commonwealth Department of Health, Dr. A. J. Metcalfe.

TABLE Ia.

The Deaths from All Forms of Cancer for Australia by Age and Sex for Certain Periods.

Age Groups. (Years.)	Males.					Females.				
	1908 to 1910.	1911 to 1920.	1921 to 1930.	1931 to 1940.	1941 to 1945.	1908 to 1910.	1911 to 1920.	1921 to 1930.	1931 to 1940.	1941 to 1945.
0—	64	193	247	218	127	52	149	188	182	110
15—	48	150	191	250	109	47	142	141	197	121
25—	80	403	423	538	272	138	601	600	673	402
35—	348	1157	1331	1475	709	581	2002	2527	2782	1396
45—	938	3632	3767	4413	2283	952	4062	5159	6234	3451
55—	1160	6060	8546	9105	5143	985	4769	7007	8451	5188
65—	1388	5512	9684	13,704	7040	1030	4137	6698	10,040	6087
75+	786	3225	4798	8783	5786	633	2797	4243	7252	5123
Unclassified ..	7	18	23	4	0	1	8	5	1	0
Total ..	4819	20,350	29,010	38,490	21,469	4419	18,667	26,628	35,812	21,878

TABLE IB.

The Deaths in Australia from All Cancers Consolidated into Broad Age Groupings.

Age Groups. (Years.)	Males.					Females.				
	1908 to 1910.	1911 to 1920.	1921 to 1930.	1931 to 1940.	1941 to 1945.	1908 to 1910.	1911 to 1920.	1921 to 1930.	1931 to 1940.	1941 to 1945.
15 to 44 ..	476	1710	1945	2263	1090	766	2745	3268	3652	1919
45 to 74 ..	3486	15,204	21,997	27,222	14,466	2967	12,968	18,924	24,725	14,726

the 1933 Australian Census. The first of these two populations has been used in a great number of statistical offices throughout the English-speaking world for many years. It has the defect of containing relatively too few old people, for England and Wales in 1901 had just passed through a period of very rapid population growth. This defect of old persons is serious when cancer rates are studied, since, of course, cancer is predominately a disease of the elderly.

Standardization onto a Life Table Population.

The life table population is of some interest, since it represents a population which would eventuate if a fixed number of births *per annum* occurred into a population, and if this population was submitted to mortality rates in general equal to those of the Australian population at the time of the three years about the 1933 Census—namely, 1932 to 1934. We can get a good idea of the proportion of the population who would eventually die of cancer at the rates of mortality existing at any time by standardizing both the total mortality and the cancer mortality onto the life table population and obtaining the ratio between the standardized rates.

Technique of Standardization.

The details of standardization are as follows. We know the number of males or females in the standard million who are in any age group. For each age-group we determine the number who would be expected to die if the death rates in this group were the same as in the corresponding age group of the actual population. The arithmetic is illustrated in Table IV, and explained by a note at the bottom of the table. These deaths in the standard life table population may be regarded in a slightly different manner as representing the deaths in a certain cohort of persons passing through life. The number of deaths observed in such a cohort of persons followed through life will reach a maximum at some age and then decline, even though the mortality rates continue to rise throughout life as far as they can be followed with accuracy.

The Priority of Cancer Under the Coding Practice of the Statistical Offices.

Elsewhere I hope to discuss in greater detail the general principles of coding and classification of deaths from the death certificates by the statistical offices. Here I merely mention that the cancers have a high priority—that is, are high in the list of diagnoses to be preferred if more than one cause should appear on the death certificate. In fact, cancer will be preferred to practically any other cause of death on the death certificate with the exception of violence and certain of the rarer specific infective diseases. Thus the appearance of the diagnosis "cancer" on a death certificate will almost certainly result in the death's being assigned to one of the rubrics of the International List devoted to cancer. It is difficult to determine how large a loss there is from the cancer rubrics because of deliberate failure to diagnose cancer on the part of the certifying medical officer for social reasons, but it is probably small. A more important source of loss in the past was the use of vague terms in diagnosis such as "senility". In the years 1911 to 1920 this was a frequent diagnosis, for we find that the mortality from "senility" was, for males over the age of sixty-five years, some 21,600 per million *per annum*. In the 1921 to 1930 period, this rate had fallen to 12,020 per million *per annum*. Certification by the coroners in cases of sudden death and in the absence of a doctor has also resulted in some cancer deaths' appearing as deaths due to "natural causes", since the coroner may be interested only in establishing that the death was a natural one and not due to any form of violence such as would require further activity on his part. It is difficult also to give any numerical value to the effect of improved diagnosis in recent years because of the greatly increased use of X rays, pathological techniques, biopsy and endoscopy, and the general increase in interest in malignant disease, since surgical treatment can now be attempted in a far greater range of cases than was possible in earlier years. Further, the frequency of autopsy is higher now than in earlier years. We may assume that in recent times there is a greater possibility than there was in the past that a patient with a cancer will be given that diagnosis, either clinically or at autopsy.

The Age-Specific Mortality from Cancer.

In Table IA are given the total numbers of deaths from cancer in Australia for the five periods chosen for study. These are not of any great comparative value, but give an idea of the absolute magnitude of the cancer problem at each period and serve as a useful check on further computations. It is usually considered of interest to give the cancer deaths as a proportion of all deaths. In Table IB I have also given the deaths in broader age groups, to reduce the number of comparisons which would be necessary if the ten-year age groups were used. I have then expressed the proportion of cancer deaths divided by all deaths in these broad age groups as a percentage in Table II.

TABLE II.

Deaths from All Cancers, in Broad Age Groups, as a Percentage of the Deaths from All Causes in the Same Age Group.

Age Groups. (Years.)	Males.					Females.				
	1908 to 1910.	1911 to 1920.	1921 to 1930.	1931 to 1940.	1941 to 1945.	1908 to 1910.	1911 to 1920.	1921 to 1930.	1931 to 1940.	1941 to 1945.
0 to 14 ..	0·30	0·25	0·38	0·50	0·58	0·30	0·24	0·38	0·55	0·66
15 to 44 ..	3·11	2·87	3·62	4·63	5·90	5·73	5·57	6·92	8·77	10·88
45 to 74 ..	12·15	12·88	15·22	15·29	14·19	16·55	17·77	19·88	19·84	20·10
75+	6·08	6·51	8·87	10·64	10·45	6·70	6·72	8·33	9·35	9·25
All ages ..	6·15	6·67	9·12	10·89	10·85	7·63	8·26	10·91	12·92	13·43

TABLE III.[1]

The Age-Specific and Sex-Specific Death Rates for All Cancers, the Deaths per Annum per Million Years of Life Experienced by Persons of the Same Age and Sex.

Age Groups. (Years.)	Males.					Females.				
	1908 to 1910.	1911 to 1920.	1921 to 1930.	1931 to 1940.	1941 to 1945.	1908 to 1910.	1911 to 1920.	1921 to 1930.	1931 to 1940.	1941 to 1945.
0–	31	25	27	24	28	26	19	21	21	26
15–	35	33	36	41	35	36	31	27	33	39
25–	74	98	89	98	92	138	148	127	130	139
35–	408	351	314	316	278	765	648	625	596	574
45–	1337	1396	1231	1106	1049	1718	1805	1807	1614	1549
55–	3468	3762	3736	3445	3160	3559	3447	3401	3253	3170
65–	7058	7006	7983	8374	7995	5766	5757	6090	6072	6315
75+	8674	9990	11,950	14,085	14,678	8001	8713	9777	10,539	10,813
All ages ..	724	808	950	1123	1180	715	771	907	1069	1215

[1] The sex-specific and age-specific death rates from cancer are calculated with the aid of the formula $R = D/E$, where R is the age-specific death rate from cancer for persons of a given age and sex, D is the number of deaths recorded in a calendar period for this sex and age group, and E is the number of years lived by persons in this age group in the corresponding period. E has been calculated by the summation of the estimated populations of the age group for June 30 each year.

I have not bothered to standardize the mortality in these broad age groups, as has been done in their studies by the Metropolitan Life Assurance Company, as it would mean a greater expenditure of time than I can spare. I consider that the procedure adopted is sufficient for the purpose—that is, to give an idea of the relative importance for broad age groups of cancer as a cause of death. I have made all other comparisons between the populations of Australia at different times by the aid of the age-specific rates and the standardized rates derived from them. These tables show that cancer is an important cause of death at all ages, except in childhood, but particularly so at the ages forty-five to seventy-four years; in this age group in the later of the periods studied it accounts for some 15% of the male and some 20% of the female deaths. For every period in the earlier age groups the cancers are a less important cause of death, even though the deaths from all other causes are relatively light. At the higher ages—over seventy-five years—the relative importance of cancer as a cause of death is less because of the greatly increased mortality from the other degenerative diseases at these ages. In Table III the age-specific death rates are shown. It is apparent that these age-specific rates continue to rise throughout life. In other words, the number of cancer deaths *per annum* that would occur in groups of a million persons exposed to risk at each age increases with age. This conclusion holds even if the group seventy-five years and upwards is further refined and divided into five-yearly age groups. In any actual population there are thus two factors to be considered if we are studying total deaths by age—firstly, the rates increase steadily with age, and secondly, there will usually be a diminished number of persons at risk at the higher ages. The age at death will thus have a frequency distribution with a mode depending on the age distribution of the population. It may be argued that the age distributions of actual populations are only the result of chance happenings in the past, so that the modal age at death and the age distribution of cancer in an actual population are matters of small scientific interest when comparisons are being made.

An age distribution of cancer deaths of more interest is that imagined to occur in a life table population. It is easily shown that this age distribution is the same as that of the deaths of a cohort of persons imagined to be followed from birth throughout life until all are dead, and submitted to the cancer rates of the observed population and the total death rates of the population on which the life table had been founded. The expected number of deaths at each age group is shown in Table IV.

The Unstandardized or Crude Death Rate from Cancer.

In a previous study on the Australian cancer mortality rates, M. J. Holmes (1925) gave the crude rates of death from cancer for all Australia and the individual States. It is necessary in any critical study to use the individual age-specific and sex-specific rates or the standardized rates derived from them. We have seen, for example, that the crude rates at any time differ from the rates standardized onto either of our standard populations, and that this depends only on a difference in age distribution, and so we should be very careful not to base any conclusions on the crude rates. However, Holmes drew conclusions from the crude rates and suggested that there was a real and serious increase in the death rates from cancer. We see from Table III that the crude rate for males has increased

TABLE IV.[1]

Standardization.

Age Groups. (Years.)	Number of Males in the Life Table Population.	Death Rates for Males in the Actual Population as Rates per Million *per Annum*.	Number of Deaths in the Standard Population.	Number of Females in the Standard Population.	Death Rates for Females in the Actual Population as Rates per Million *per Annum*.	Number of Deaths in the Standard Population.
0–	221,691	24	5	211,607	21	4
15–	144,491	41	6	138,995	33	5
25–	141,010	98	14	135,816	130	18
35–	136,146	316	43	131,323	596	78
45–	127,312	1106	141	124,446	1614	201
55–	109,614	3445	377	112,130	3253	365
65–	78,255	8374	655	88,050	6072	535
75+	41,481	14,085	584	57,633	10,539	607
Total ..	1,000,000	1123	1825	1,000,000	1069	1813

[1] The standard populations have been computed from the life tables constructed from the data of the 1933 census in Australia. The members of the standard population have been imagined to be submitted at each age group to the same mortality rates from cancer as obtained in the actual population of Australia in the years 1931 to 1940.

from 724 per million *per annum* to 1180 and that the crude rate for females has risen from 715 to 1215. An inspection of the age-specific rates shows that, in general, the rates have not risen, with the possible exception of the rates at the age-groups over seventy-five years, in which groups, it may be suggested, the effect of more precise diagnosis in recent times is most likely to be apparent. It is probable that the crude rates of mortality from cancer will continue to rise for some time as the population ages further and the age distribution approximates more closely to that of a life table population.

TABLE V.

The Crude and Standardized Death Rates from Cancer as Rates per Million per Annum.

Period.	Crude Rates of Mortality from all Cancers.		Rates Standardized onto the Population of England and Wales, 1901.		Rates Standardized onto the Life Table Populations, Australia, 1933 Census.	
	Males.	Females.	Males.	Females.	Males.	Females.
1908 to 1910 ..	724	715	713	834	1540	1711
1911 to 1920 ..	808	771	744	829	1626	1733
1921 to 1930 ..	950	907	775	849	1753	1813
1931 to 1940 ..	1123	1069	786	831	1825	1813
1941 to 1945 ..	1180	1215	755	835	1777	1833

Teece (1901) attempted to show that there had been a real increase in the frequency of deaths from cancer in Australia, using an insured population and also the crude rates from the various Australian colonies. In the discussion which followed he was warmly criticized, and it was pointed out that in comparing two populations it was not enough to ensure that they had the same mean age —they must also have the same age-distribution. If they did not have the same age-distribution, then some form

TABLE VI.

The Proportion of Deaths in the Standard Populations Due to Cancer Expressed as a Percentage of All Mortality in the Same Standard Population.

Period from which Rates were Derived.	The Percentage of All Deaths Due to Cancer.			
	Standard Population Used, England and Wales, 1901.		Standard Populations Used, Australian Life Table Populations (1933).	
	Males.	Females.	Males.	Females.
1908 to 1910 ..	6·2	8·3	7·9	9·8
1911 to 1920 ..	6·4	8·5	8·5	9·9
1921 to 1930 ..	8·2	10·4	10·8	11·8
1931 to 1940 ..	9·4	11·7	11·8	12·8
1941 to 1945 ..	9·6	12·4	11·5	13·1

of standardization was essential. Finally, King and Newsholme (1901) had reprinted their article on "The Alleged Increase of Cancer", in which it was shown for England and Wales and for Frankfurt that the apparent increase of cancer was due to aging of the population and to an increased facility in diagnosis of cancer in inaccessible regions.

The Standardized Death Rates.

It is convenient to have some single rate that will give an estimate of the cancer mortality at all ages, and at the same time remove the effect of any special feature of the age distribution of the population studied. Such a single rate is given by the standardized rate. I have treated the two sexes as two different populations and have given standardized rates per million for each sex. It will be seen from Table V that if the male or the female mortalities are standardized onto the population of England and Wales of 1901; then the standardized rates have not risen over the total period 1908 to 1945. It is possible that the actual or census population of England and Wales of 1901 may be regarded as quite an unsuitable population for standardization of the cancer rates, since the older persons are so poorly represented in it. To meet this criticism the rates can be standardized onto the life table population constructed after the 1933 census of Australia. There was an increase in the standardized rates between the period 1911 to 1920 and the next decade, but since then it would appear that these rates have remained stationary. Further examination of the age-specific rates shows that

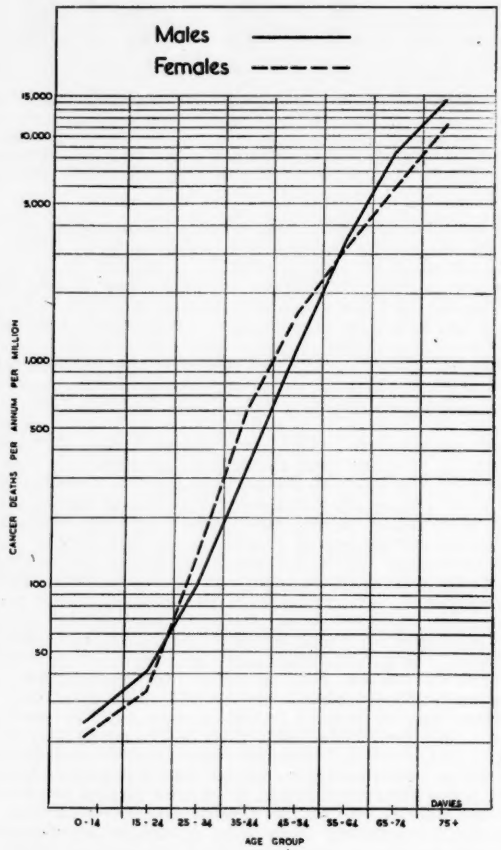

FIGURE I.

Cancer mortality in Australia. The age-specific cancer mortality rates per million *per annum* for each sex for the period 1931 to 1940. Semilogarithmic grid.

this increase is almost entirely accounted for by the increases at the very high ages, at which ages, as has already been pointed out, there is most reason to suspect that there have been the greatest changes in diagnosis and certification.

The Proportion of Deaths due to Cancer.

If we divide the crude cancer death rate by the crude death rate due to mortality from all causes, we obtain a ratio that has risen consistently from 1908 to 1945. The same conclusion holds when the rates are standardized, as is shown in Table VI. In general we may say that these ratios have risen more because of changes in the total mortality than because of changes in the cancer mortality. The most important result to record is that at the rates of cancer mortality in 1931 to 1940 and the general mortality rates prevailing at that time (the rates for the years 1932-1934 were used to construct the 1933 life tables)

about 11·8% of males and 12·8% of females would finally die of cancer.

Factors Affecting the Total Cancer Rates.

Age.—Tables I to III all bear out the well-known observation that cancer is predominantly a disease of later life. The mortality rates for cancer as a whole continue to increase throughout life.

Sex.—Sex has an important bearing on the cancer rates, since in the female population cancers of the breast and of the female genital organs contribute a considerable proportion of the whole cancer mortality, and especially so at the ages under forty-five years. In the male population, at the higher ages, the mortality from prostatic cancer is appreciable. However, we cannot consider fully the effects of sex until we discuss in more detail the mortality from individual organs or systems in the two sexes. With this limitation in mind, the ratio of the male rate to the female rate at each age has been computed and expressed as a percentage in Table VII. This shows that in 1931 to 1940 the male rate was 75% of the female rate at ages twenty-five to thirty-four years, and only 53% at thirty-five to forty-four years. At ages fifty-five to sixty-four years the sexes have approximately equal rates, and over the age of sixty-five years the male rates are greater than the female.

The comparison of the male and female rates by age has been made graphically in Figure I.

Race.—The Australian statistics cannot give any direct information on the subject of incidence of cancers by race, except to express the mortality of a predominantly northern European stock in a tropical and subtropical climate. It is worth while to note here that the Australian statistics do not include the deaths of full-blooded aborigines, but do include some deaths of half-castes. The number of these latter in any case is not great.

Occupation.—With regard to occupation, again the Australian statistics will not be found very helpful, as it will be found impossible to obtain suitable divisors for the deaths recorded in the various occupational groups.

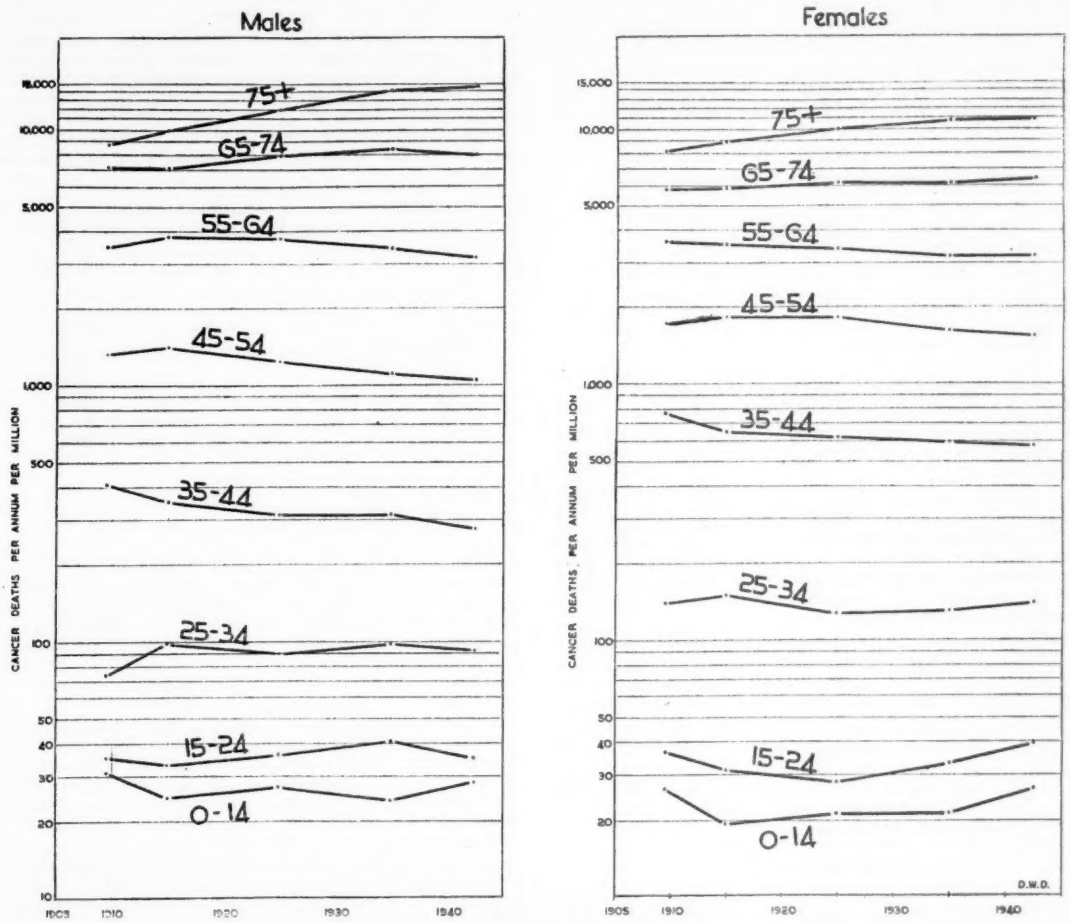

FIGURE II.

Cancer mortality in Australia. The trends of the age-specific mortality rates for cancer in Australia. The cancer mortality rates are given as a rate per million *per annum*. Semilogarithmic grid.

Parity.—The parity of women who die from cancer is tabulated in special tables in *Demography*, which give the age, marital state and parity of the females. I shall analyse these in some detail when I come to the study of the cancers of the female breast and the female genital organs on another occasion.

The Type of Growth.—In one of the supplementary tables of *Demography* the age and sex distributions of the type of cancer are given according to site. Two types are of some interest—namely, sarcoma and melanoma—but I shall have to defer consideration of them to a further article.

The Trend of Cancer Mortality.

I find, as did Cumpston (1936) in a previous survey, limited to a discussion of the years 1911, 1921 and 1933, that over the period considered there has been no rise in the mortality rates from cancer (all forms) in Australia, with the rather doubtful exceptions of those for the age groups over seventy-five years, when the mortality for the periods 1908 to 1910 and 1911 to 1920 is compared with the mortality rates of the three later periods. I have given reasons for doubting the reality of this increase. I have displayed in Figure II the trends of the age-specific mortalities for each sex. It can be seen that there has actually been a decrease in the mortality in the ages thirty-five to fifty-four years in both sexes. It is apparent that we must put aside the conclusion of M. J. Holmes (1925) that there had been or is a real and serious increase in the death rates from cancer in Australia. It is clear that we can forecast an increase in the crude rates with aging of the population, such as would seem to be inevitable in the future. We may expect, in the absence of any dramatic new therapy or changes in the method of diagnosis and certification, that the crude rates will tend to rise toward the life table death rates from cancer—that is, we may expect rates of the order of 1800 per million *per annum*.

TABLE VII.

The Male Cancer Rate Expressed as a Percentage of the Female Rate (Based on the Mortality Rates for 1931–1940.

Age Groups. (Years.)	$\frac{\text{Male Rate of Mortality}}{\text{Female Rate of Mortality}} \times 100$.
25–	75
35–	53
45–	69
55–	106
65–	138
75+	134

Summary.

1. The total deaths from cancer for the two sexes, given in the official statistics for Australia, 1908 to 1945, have been summarized and cancer has been shown to be the cause of an important proportion of the total deaths at all ages above fifteen years.

2. Comparisons of the age-specific death rates from cancer (all forms) and the standardized rates for five periods have been made. The age and sex distribution of the mortality from cancer (all forms) has been displayed.

3. The general conclusion is drawn that there has been no certain increase in cancer mortality over the period studied. In fact, there has been a decline at ages thirty-five to fifty-four years in both sexes. Over seventy-five years of age there has been an increase in the cancer rates, but this is possibly spurious.

Acknowledgements.

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CHILDHOOD TUBERCULOSIS IN QUEENSLAND.

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Brisbane.

THE first half of the twentieth century has witnessed encouraging attempts by the medical profession to combat tuberculosis in all parts of the civilized world. Increased vigilance on the part of doctors has led to the earlier detection of subjects and to the subsequent treatment and isolation, which have helped to prevent the spread of the disease. The result has been, in Osler's metaphor, to reduce the amount of "seed" scattered by the sower. Less progress has been made with the study of those variable factors such as climate, food and housing, which affect the "soil". It is well known in a general way that prosperity, sunshine, fresh air and protective foods make tuberculous infection less likely, but precise knowledge is lacking as to which, if any, particular factor is the most important.

TABLE I.

Incidence of Tuberculosis at the Brisbane Children's Hospital.

Year Ending June 30.	Tuberculosis Cases.	Total Admissions.
1940	5	3494
1941	9	5112
1942	6	4907
1943	8	5562
1944	4	6738
1945	10	6252
1946	6	6862
1947	7	7299
1948	4	7407
1949	5	6897
Total ..	64	60,530

A possible approach to this problem is to find a region in which tuberculous infection is relatively scarce and to analyse the various components of the environment in such a region. Comparisons can then be drawn with the environmental components of other areas which are similar in many ways but have a higher tuberculosis rate.

There is reason to believe that—at least so far as children are concerned—Queensland has one of the lowest tuberculosis rates in the world, and that fewer children are affected proportionately than in the other capital cities of Australia. If these beliefs can be upheld, a useful starting-point for such an environmental survey will have been gained.

In this preliminary paper figures are presented from the five largest children's hospitals in Australia to substantiate this claim.

The Brisbane Children's Hospital, which admits patients from birth to the age of twelve years, has 235 beds for public patients. It serves about two-thirds of the Brisbane metropolitan area (population 405,000), as well as functioning as a base hospital for southern Queensland and the extreme north of New South Wales. Table I sets out the number of children suffering from tuberculosis who have been admitted to the wards of the Brisbane Children's Hospital during each twelve months of the ten-year period from July 1, 1939, to June 30, 1949. All forms of tuberculosis are included. Each child's name has been counted

once only for the year during which he was first admitted, no matter how numerous his subsequent visits to hospital. The adjacent column, headed "Total Admissions", includes both admissions and readmissions, and therefore refers to a slightly smaller number of children than the figures indicate.

The sceptical reader, confronted with figures showing a tuberculosis incidence of little over one per thousand hospital admissions, might say that most of the Brisbane cases of childhood tuberculosis probably escaped detection. One could contend in reply that the powers of observation of Brisbane physicians were no doubt as keen as those of their colleagues elsewhere, and that if one could strike an average of the clinical acumen of its staff there would probably be little to choose between one large hospital and another in the matter of diagnostic skill. Liberal use is made in Brisbane of the Mantoux test, although it is not performed upon every child as a routine measure. In the event of a positive result, every effort is made to locate the lesion. Finally, a post-mortem examination is made upon the majority of deceased patients, yet only once in ten years has significant tuberculous disease been found that was undetected during life.

It is possible that a few children mildly affected with tuberculosis and attending as out-patients were not discovered; but the proportion of such missed diagnoses should not be higher in Brisbane than elsewhere. On the other hand, it is most unlikely that any patients discovered in the out-patient department would not at some time have secured admission to the wards, for it has been customary to admit them for observation and bed rest and for such procedures as gastric lavage or biopsy of a suspected gland. It may be concluded, therefore, that the figures shown comprise virtually all the tuberculous children discovered at the hospital during the period.

TABLE II.

Comparative Tuberculosis Incidence at Five Children's Hospitals.

City.	Hospital.	Tuberculosis Admissions, Ten-Year Period 1.7.39 to 30.6.49.	Total Admissions, Ten-Year Period 1.7.39 to 30.6.49.	Tuberculosis Rate per 1000 Admissions.
Melbourne	Children's Hospital.	625	62,680	9·97
Perth ..	Princess Margaret Hospital.	360	56,199	6·41
Adelaide	Children's Hospital.	301	50,513	5·96
Sydney ..	Royal Alexandra Hospital for Children.	350	91,793	3·81
Brisbane	Children's Hospital.	64	60,530	1·01

As has been stated already, particular interest attaches to the figures for the incidence of childhood tuberculosis in other parts of Australia. By the courtesy of the medical superintendents of the institutions concerned, who have supplied the figures from their records departments, it has been possible to prepare a table showing the comparative incidence of tuberculosis at the five principal children's hospitals in Australia. The results are set out in Table II.

Although these figures are roughly comparable, some latitude must be allowed in their interpretation. It is obvious that, at different hospitals, different criteria may govern the admission of tuberculosis patients to the wards. For example, children with tuberculous cervical adenitis may at one hospital be treated conservatively as out-patients, and at another be admitted for excision operations. Only those children admitted to the wards have been considered here, as accurate out-patient statistics are unavailable. Secondly, the control over the admission of ordinary patients to beds in the wards is stricter in some hospitals than in others, and in the same hospital at different times, strictness being enforced by staff shortages, war-time difficulties and so forth. A tendency to treat patients with some types of tuberculosis as out-patients would lower the "tuberculosis rate", as would leniency shown by the casualty officers in admitting numbers of patients of all types to the wards.

As an additional check upon the frequency of occurrence of childhood tuberculosis, and as a means of affording comparison with children's hospitals elsewhere, the figures for tuberculosis may be contrasted with those for some other common disease. Table III shows a comparison between tuberculosis and intussusception admissions to the Brisbane Children's Hospital during the five-year period from July 1, 1944 to June 30, 1949. Intussusception was selected as a condition which is clear-cut, unaffected by environment and certain to secure for its victim a hospital bed.

TABLE III.

Comparison between Tuberculosis and Intussusception at the Brisbane Children's Hospital.

Year Ending June 30.	Tuberculosis Admissions.	Intussusception Admissions.
1945	10	9
1946	6	11
1947	7	8
1948	4	11
1949	5	5
Total ..	32	44

As will be evident from Table III, more patients have been treated for intussusception than for tuberculosis during the past five years at the Brisbane Children's Hospital, the ratio being approximately four to three. There must be very few hospitals to which this ratio applies.

The tuberculosis death rate shows considerable variation when figures from the different children's hospitals of Australia are compared (Table IV), that for the Royal Alexandra Hospital for Children, for example, being almost four times as high as the rate at the Princess Margaret Hospital. One explanation for this may be that benign tuberculosis of the cervical glands (220 out of the 360 Perth cases) is less likely to qualify a child for admission as an in-patient at some hospitals than at others. Even so, the mortality rate in Brisbane is a great deal higher than in Perth. When cases of cervical adenitis are excluded, the Brisbane Children's Hospital has 15 deaths from 34 cases, whereas the Princess Margaret Hospital has 29 deaths from 140 cases. It must be concluded that, whatever the beneficent influences in the Queensland environment, they act in the direction of reducing the incidence of tuberculosis and not of improving the capacity of children to destroy tubercle bacilli once the disease is acquired.

TABLE IV.

Tuberculosis Mortality at Five Children's Hospitals in the Ten-Year Period July 1, 1939, to June 30, 1949.

City.	Hospital.	Tuberculosis Admissions.	Tuberculosis Deaths.	Death Rate. (Percentage.)
Perth ..	Princess Margaret Hospital.	360	29	8·1
Adelaide	Children's Hospital.	301	51	16·9
Brisbane	Children's Hospital.	64	15	23·4
Melbourne	Children's Hospital.	625	147	23·5
Sydney	Royal Alexandra Hospital.	350	110	31·4

In a subsequent paper an attempt will be made to analyse some of the factors in the environment of the children of southern Queensland, which may be responsible for the low tuberculosis infection rate. Meanwhile, it is hoped that this preliminary communication will stimulate fresh interest in the problem of the eradication of the disease.

HÆMOGLOBIN DETERMINATIONS OF 1265 BUNBURY SCHOOL CHILDREN AND OF A SMALL GROUP OF ADULTS.

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REPORTS of a high incidence of anæmia in the south-west of Western Australia, in addition to various theories for its existence, prompted a hæmoglobin survey amongst school children in that area.

As very few figures have been published for Australian children, the findings for one section of this survey are presented in this paper. A short summary of recent developments in hæmoglobinometry in Great Britain precedes these figures, as they are directly comparable with those based on the British Standards Institution colour standard. It also serves to stress again the importance of selection of method and apparatus when hæmoglobin surveys are undertaken.

When the literature is read it is found that the most consistent statement expressed on hæmoglobinometry in the past fifty years has been similar in context to that given by Haden (1922), when he commenced his paper as follows:

> The clinical estimation of hemoglobin has always been a most unsatisfactory procedure . . . .
>
> There are numerous technical difficulties in the way of accurate hemoglobin work. Perhaps the greatest two obstacles, however, have been the lack of a simple method of calibration for hemoglobinometers and the absence of a uniform standard. All hemoglobinometers are graduated to read in percentages, yet there is no agreement as to what the 100 per cent. shall be equivalent.

It is now possible to reduce these difficulties to a minimum by the use of improved hæmoglobinometers, and by methods which no longer rely on dilution and on the visual matching of colours. Facilities for calibrating instruments and glassware are also more readily available. In Australia, however, too many estimations are made still by operators who use crude types of instruments, and who have not been tested for ability to match colours, or for consistency of an accurate technique; and too many instruments are in use which have not been calibrated by approved methods. These things may not be of great importance in the work of a general practitioner, but surely they must be so in all pathological laboratories and to those conducting hæmoglobin surveys.

Recent Developments in Hæmoglobinometry.

For many years, in Britain, the Haldane-Gowers apparatus has been in general use, and results have been expressed as percentages of the original Haldane standard, that is, 13·8 grammes of hæmoglobin per 100 millilitres equals 100%. The use of this scale in Britain has meant that many of the hæmoglobin determinations made in that country were lower than in other comparable parts of the world (Wardlaw, 1941; King *et alii*, 1944; Macfarlane *et alii*, 1944). In order to overcome several shortcomings of other methods, Clegg and King (1942) developed the alkaline hæmatin method in conjunction with crystalline hæmin as a standard. Subsequent work with this method also made it apparent that there was a possible error in the Haldane standard.

With this accumulating evidence against the most commonly used of Britain's hæmoglobin determination techniques, a complete investigation was undertaken, during which a permanent British Standards Institution colour standard and an efficient comparator for its use were established at the National Physical Laboratory, London, by Donaldson, Harding and Wright (1943). After exhaustive tests this colour standard was found to be equivalent to a hæmoglobin concentration of 14·8 grammes *per centum* of blood by iron determinations, or to 14·4 grammes *per centum* by oxygen capacity determinations (Macfarlane *et alii*, 1944; King *et alii*, 1944, 1948). As carbon monoxide capacity measurements gave figures approximating those obtained by iron determinations, 14·8 grammes *per centum* is taken to be the hæmoglobin equivalent for this standard (King *et alii*, 1947).

The new British Standards Institution colour standard was prepared so that it agreed with Haldane's original definition for it, but it was standardized in terms of colour by a photoelectric spectrophotometer and only indirectly in terms of oxygen capacity. The discrepancy in the original Haldane standard is explained by the fact that the gasometric apparatus devised by Haldane gives consistently lower results than the more modern Van Slyke method (King *et alii*, 1947).

The corrected Haldane scale brings British hæmoglobin value figures into line with those in America and other parts of the world.

Tests made during this investigation show that methods for determining hæmoglobin values based on acid hæmatin are the least reliable (King *et alii*, 1947, 1948), while those based on oxyhæmoglobin or cyan hæmatin are the most reliable. Alkaline hæmatin was recommended for photoelectric instruments only.

In summarizing the results of precision tests on clinical hæmoglobinometers, Macfarlane, King *et alii* (1948) found that those instruments involving dilution (for example, those of Haldane, Gowers, Sahli) were the least reliable for determining hæmoglobin values. It is stated that a difference of 10% in readings must be found for it to be significant. The actual methods involving use of whole blood were also found to be slightly superior to those based on dilution. The Sahli-Zeiss, with its moving wedge standard, was found to be the best of the proprietary methods, even though based on acid hæmatin.

However, this instrument was displaced for pride of place among clinical hæmoglobinometers by the new Medical Research Council grey wedge photometer (King *et alii*, 1948), which was developed and subjected to precision tests during the year of the British investigation. It has added advantages of being graduated in terms of the British Standards Institution colour standard and of estimating oxyhæmoglobin instead of the less accurate acid hæmatin. Its manipulation is also said to be simple and quick.

The advent of less expensive photoelectric apparatus provides yet another way of overcoming the inherent errors of dilution methods and the inaccuracies of crude visual colorimeters. However, in inexperienced hands, and if used without careful standardization, these instruments can be as inaccurate as any hæmoglobinometer. There are patent photoelectric hæmoglobinometers being manufactured for which there is no method of checking the standardization in the laboratory. These have been found on occasion to give grossly incorrect results.

Normal Hæmoglobin Levels for Children.

Owing to the many and varied scales from which hæmoglobin values are read, comparisons of one set with another must be made with the utmost caution. It is well to establish the principle of never accepting hæmoglobin values given in grammes until one is certain that they were directly determined as such, or knows the scale from which they were converted. In the case of conversions from the Haldane scale, it must also be known whether the original or the British Standards Institution colour standard corrected value was used.

Breinl and Priestly (1914) carried out hæmoglobin estimations on 574 school children, aged seven to fifteen years, living in tropical Queensland, and reported the average figure as similar to that for normal children in temperate climates. They used two Fleischl-Miescher hæmoglobinometers, which they standardized with a Haldane instrument, which in turn had been checked for accuracy by oxygen-capacity determinations with the Haldane ferricyanide method. They stated that when converting hæmoglobin values to grammes they used the scale on which 13·8 grammes *per centum* is equivalent to 100%. In the light of the corrected British Standards

Institution colour standard, the average for children aged seven to fourteen years, as deduced from information in their tables, is close to 13·2 grammes *per centum*.

In New Zealand, Hayes (1945) determined hæmoglobin values for 520 children, aged five to thirteen years, and found a mean of 12·5 grammes *per centum*. He used a Sahli hæmoglobinometer and checked it against a Haldane, in which he used a new British standard specification tube. In a favourable comparison of his results with those of other workers, however, it is apparent that the British Standards Institution colour standard correction was not applied to the results of three out of five of these workers (Table I). No data are available for checking the other two. It is probable that Hayes's mean of 12·5 grammes *per centum* should be 13·4 grammes *per centum* if corrected for the British Standards Institution standard, but again insufficient data are available to verify this.

TABLE I.

Worker.	Hæmoglobin Value.		
	Per Centum. (Original.)	Grammes *per Centum* when 13·8=100% (Hayes).	Grammes *per Centum* when 14·8=100% (British Standards Institution Colour Standard Correction).
Davidson (1935) ..	95	13·0	14·1
Whitby and Britton (1939)[1]	90–100	12·5–13·8	13·3–14·8
Davidson (1942) ..	95±5	12·5–13·8	13·3–14·8

[1] The fourth edition (1944) of their book gives identical figures.

In 1943 a hæmoglobin survey was undertaken in Great Britain (Medical Research Council, 1945). It was one of the most extensive and thorough of its kind. Every effort was made to achieve accurate results and to eliminate technical and personal errors. The Haldane-Gowers hæmoglobinometer was used, but all colour tubes, graduated tubes and pipettes conformed to specifications set out by the National Physical Laboratory, London. Results were expressed in terms of the British Standards Institution colour standard, and all persons taking part in the survey underwent thorough tests for accuracy.

Hæmoglobin Determinations in Bunbury, Western Australia.

Technical Aspects.

An "Eel" photoelectric colorimeter was used for measuring the colour density of solutions of alkaline hæmatin. An inorganic standard originally described by Gibson and Harrison (1945) was also used.

The "Eel" Photoelectric Colorimeter.—The model of the colorimeter used on this survey was adapted for use with a small dry type accumulator. This lit a 2·2-volt bulb, which sent a beam of light through a tricolour green gelatin filter and then through the test solution contained in glass test tubes provided with the instrument. The emergent light passed to the single selenium barrier-layer type photoelectric cell. The current so generated deflected the needle of the microammeter and enabled a direct reading to be taken on the logarithmic scale.

The Standard.—The inorganic standard was prepared by the method described as the "simplified method of preparation" by Gibson and Harrison (1945). They found the equivalent hæmoglobin value to be 16·0 ± 0·2 grammes *per centum* by iron determinations. The solution prepared for the Bunbury survey was found subsequently to have a value of 15·9 grammes *per centum*, but in the reading of hæmoglobin values this was taken as 16·0 grammes *per centum*. (See remarks below on calibration of the colorimeter.) Before use a portion of the standard was diluted by adding an equal quantity of distilled water. This was necessary, as full strength gave readings on the less accurate section of the logarithmic scale of the microammeter. The closed flasks of diluted standard were heated in a boiling water bath for five minutes and then cooled in iced water to 18° C. immediately before use. It was necessary to reheat these, or fresh portions of the diluted standard, after one hour had elapsed, to ensure equilibrium of the two modifications of chromium sulphate. Prior to the undertaking of the survey, series of dilutions of the standard were prepared and read in the "Eel" photoelectric colorimeter. The readings so obtained showed that Beer's law held within the range to be used. Hæmoglobin values for the blood samples were read direct from the straight line drawn for the purpose. The ordinates on the graph paper represented grammes of hæmoglobin *per centum*, and the abscissæ the ammeter readings. The line was drawn from zero through the point representing the standard.

Calibration of the Colorimeter.—The Red Cross Blood Transfusion Service laboratory in Sydney was visited on completion of the survey. The sensitive photoelectric instrument used by that laboratory was reading in accordance with a calibration based on the British Standards Institution colour standard value of 100% = 14·8 grammes of hæmoglobin *per centum*. This calibration had been effected by means of an exchange of blood samples by air with the National Physical Laboratory, London. In order to recheck the technique, the instrument and the standard used in the Bunbury survey, hæmoglobin determinations were made on 17 samples of oxalated human blood, the same procedure being used as in the field. The Red Cross laboratory also determined the values of these samples by means of an oxyhæmoglobin method and their photoelectric instrument. The 17 hæmoglobin values, as determined by the Red Cross laboratory, were plotted against the 17 microammeter readings obtained by using the "Eel" photoelectric colorimeter. In this way the Gibson-Harrison standard was found to have an equivalent value of 15·9 grammes of hæmoglobin *per centum*. The hæmoglobin values obtained for the Bunbury survey are thus considered to be directly comparable with figures obtained in Great Britain during the 1943 survey, as both are based on the British Standards Institution colour standard value of 100% = 14·8 grammes of hæmoglobin *per centum*.

Procedure Adopted and the Alkaline Hæmatin Method.—During the last weeks of the school year hæmoglobin estimations were carried out on 1265 children from the following Bunbury schools: the High School, Saint Joseph's Convent, the Sacred Heart Convent, the Senior State School, the Infants' School, the South Bunbury State School and the South Bunbury Convent. A small group of adults was included and a section on these values follows that on the children. The blood samples were collected at the schools in the morning and the hæmoglobin content of each was determined at the district hospital in the afternoon. In many cases a ready supply of blood to the fingers was ensured by rotation of the arm from the shoulder. The 0·05 millilitre of blood taken by a finger prick was mixed in 10 millilitres of a decinormal sodium hydroxide solution in a test tube. A 0·1 millilitre graduated pipette which had been calibrated with mercury was used. Between being used for individual subjects this was carefully washed and dried by means of water, methylated spirit, ether and hot air. On return to the laboratory the open tubes were heated in a boiling water bath for four minutes and immediately cooled in water to room temperature. The solutions were then read in order on the "Eel" photoelectric colorimeter, the tricolor green filter being used. Readings were taken of the inorganic standard at frequent intervals throughout, in addition to those taken at the commencement and finish of work.

Results of Bunbury Determinations.

In Table II are set out the mean hæmoglobin values for each age group, both for the Bunbury survey and for that of Great Britain. The figures for Britain are taken from Table XIII, on page 31 of the Medical Research Council's Special Report Series No. 252; but to facilitate comparison with the Bunbury figures the coefficients of variation have been worked out and added, and the Haldane percentages

TABLE II.
Hæmoglobin Values for Children.

Age. (Yrs.)	Bunbury Schools.						Great Britain, 1943.					
	Boys.				Girls.		Boys.			Girls.		
	Number of Subjects.	Mean Hæmoglobin Value. (Grammes *per Centum.*)	Standard Deviation.	Coefficient of Variation.	Number of Subjects.	Mean Hæmoglobin Value. (Grammes *per Centum.*)	Standard Deviation.	Coefficient of Variation.	Number of Subjects.	Mean Percentage of B.S.I. Colour Standard.	Standard Deviation.	Coefficient of Variation.[1]
5	6	13·9	0·69	5·0	10	13·9	0·60	4·3	32	89·4	7·97	8·2
6	52	13·6	0·89	6·5	60	13·4	0·79	5·9	45	91·8	8·00	8·7
7	68	13·7	0·86	6·3	55	13·8	1·02	7·4	37	90·3	12·66	14·0
8	54	13·8	0·73	5·3	63	13·6	0·83	6·1	104	92·0	12·74	13·8
9	61	14·0	0·89	6·4	66	14·0	0·91	6·5	94	91·4	6·39	7·0
10	71	13·9	0·91	6·5	65	13·9	0·81	5·8	123	91·0	6·77	7·4
11	76	14·1	0·87	6·2	56	14·0	0·88	6·3	128	92·7	6·77	7·3
12	62	14·0	1·02	7·3	65	14·2	0·87	6·1	136	94·6	8·71	9·2
13	80	14·7	1·05	7·1	72	14·4	0·92	6·4	223	97·1	6·94	7·1
14	57	15·0	1·01	6·7	64	14·5	0·80	5·5	173	97·9	7·24	7·4
15	44	15·5	1·02	6·6	32	14·5	0·80	5·5	165	101·0	7·13	7·1
16	9	15·7	0·97	6·2	12	14·8	0·71	4·8	174	103·9	7·94	7·6
17									115	104·2	5·97	5·7

Age. (Yrs.)	Great Britain, 1943.				
	Girls.				
	Number of Subjects.	Mean Percentage of B.S.I. Colour Standard.	Standard Deviation.	Coefficient of Variation.[1]	Mean. (Grammes *per Centum.*)[2]
5	41	92·7	7·65	8·3	13·7
6	48	93·4	8·55	9·2	13·8
7	46	92·2	7·97	8·6	13·4
8	59	92·8	9·39	10·1	13·7
9	70	90·8	9·98	11·0	13·4
10	76	90·6	10·90	11·6	13·9
11	84	93·0	8·69	9·3	13·8
12	144	94·5	8·51	9·0	13·8
13	134	94·3	7·59	8·0	14·0
14	73	97·7	8·04	8·2	14·5
15	79	98·2	6·50	6·6	14·5
16	82	98·7	7·38	7·5	14·6
17	34	97·4	8·18	8·4	14·4

[1] This column was converted and added to the table by the writer to allow a direct comparison with the Bunbury figures.
[2] The coefficients of variation for the British Standards Institution figures were also determined by the writer for a similar purpose. (From Table XIII, Medical Research Council Special Report number 252.)

have been converted to grammes *per centum*, the British Standards Institution colour standard value of 14·8 grammes *per centum* being used as 100%.

Table II shows a more than satisfactory hæmoglobin level for each age group of the Bunbury children, and excellent agreement between these and the children of Great Britain in 1943. No pre-school children were tested, but it is not uncommon for this group to have relatively low hæmoglobin levels. Whether this is the case in Bunbury or not, the figures show that at the age of seven years the children's hæmoglobin values have reached a satisfactory level, and that this is maintained with only a slight increase until the age of twelve years. At this age the expected increase towards adult levels commences and, as is usual, the increase for boys is greater than for girls. Before this age no sex difference in the levels is apparent.

The mean hæmoglobin level for the 1265 Bunbury school children aged five to sixteen years was found to be 14·1 grammes per 100 millilitres of blood, and for the 1049 aged five to thirteen years 14·0 grammes per 100 millilitres of blood. These figures compare more than favourably with those found by other workers and reviewed in this paper.

Table III gives the distribution of the 1265 children amongst the schools, especially in relation to those children with lower hæmoglobin values. Almost equal numbers of boys and girls were tested, and almost equal numbers had hæmoglobin values under 13·0 grammes *per centum*. However, only 10·6% of the children fell into this class, and only 0·9% into the class with levels under 12·0 grammes *per centum*. No child had a hæmoglobin value under 11·0 grammes *per centum*.

The Infants' School had the highest percentage of children with levels under 13·0 grammes *per centum*, but this is explained by the lower age groups in attendance. Similarly a large number of the children from the combined convents of Saint Joseph and the Sacred Heart, and from the South Bunbury State School were in these lower age groups, and these schools also had higher percentages of children with values under 13·0 grammes *per centum*. South Bunbury Convent, on the other hand, also with a high proportion of younger children, had only 3·8% with hæmoglobin levels under 13·0 grammes *per centum*, and none under 12·0 grammes *per centum*.

Table IV gives the frequency distribution of the hæmoglobin values for 1049 children aged five to thirteen years inclusive. Each group of hæmoglobin values extends over 0·5 gramme *per centum*. The number and percentage of children in each group are given. The frequency distribution curve is drawn from these figures, numbers of children being used as the ordinates and the midpoint of each hæmoglobin group as the abscissæ.

Adult Hæmoglobin Values.

The Red Cross Blood Transfusion Service train visited Bunbury during the course of this survey. Therefore, the opportunity was taken to estimate hæmoglobin levels on 50 of the voluntary blood donors. To these are added 18 estimations on teachers of various Bunbury schools, making a total of 68 adults.

The procedure for these estimations was similar to that used for the children, except that 16 of the blood samples were taken during the early part of the afternoon.

Of the 28 men tested, all but two were between the ages of nineteen and forty-nine years. The remaining two were aged over fifty years. All but one of these men had been living in the south-west for at least one year. Their mean hæmoglobin level was 15·9 grammes *per centum*, and the range was 12·6 to 18·8 grammes *per centum*. This range is somewhat misleading, in that only one value of 12·6 occurred, and the next lowest was 14·3.

Similar data are given for the 40 women, though it is realized that they form a heterogeneous group, which, if numbers permitted, should be subdivided according to age, pregnancies *et cetera*. Their ages fell between seventeen and forty-nine years, except for six, who were aged over fifty years. There were also six who had not lived

TABLE III.

Incidence of Hæmoglobin Levels Less than 13·0 Grammes per Centum.

School.	Age Group. (Years.)	Children Tested in Each School.			Number and Percentage of Children with Hæmoglobin Levels Less than 13·0 Grammes *per Centum*.						Number and Percentage of Children with Hæmoglobin Levels Less than 12·0 Grammes *per Centum*.					
					Total.		Boys.		Girls.		Total.		Boys.		Girls.	
		Total.	Boys.	Girls.	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
High	12–16	287	151	136	3	1·1	2	1·3	1	0·7	1	0·4	1	0·7	0	0
Saint Joseph and Sacred Heart Convents	5–16	188	66	122	25	13·3	10	15·2	15	12·3	1	0·5	1	1·5	0	0
Senior State School	9–14	308	170	138	27	8·8	20	11·8	7	5·1	2	0·7	1	0·6	1	0·7
Infants' School	6– 9	171	95	76	47	27·5	23	24·2	24	31·6	4	2·3	2	2·1	2	2·6
South Bunbury State School	5–11	206	108	98	28	13·6	11	10·2	17	17·4	3	1·5	2	1·9	1	1·0
South Bunbury Convent ..	5–14	105	50	55	4	3·8	3	6·0	1	1·8	0	0	0	0	0	0
All Schools	5–16	1265	640	625	134	10·6	69	10·8	65	10·4	11	0·9	7	1·1	4	0·6

the preceding twelve months in the south-west. However, these had all been in the area for at least five months. The mean *hæmoglobin level was 14·3 grammes per centum*, with a range of 12·6 to 15·7 grammes *per centum*.

These figures indicate a satisfactory hæmoglobin level for a selected group of adults living in or near Bunbury. It is interesting to note that not only are they in agreement with overseas values, *but that the female value is* 89·9% that of the male. Wardlaw (1941) gives evidence to show that the hæmoglobin level of normal women is 87±5% that of normal men.

TABLE IV.

Frequency Distribution of Hæmoglobin Levels for 1049 Children Aged Five to Thirteen Years.

Hæmoglobin Level. (Grammes *per Centum*.)	Children in Each Group.	
	Number.	Percentage.
11·0 to 11·4	3	0·3
11·5 to 11·9	8	0·8
12·0 to 12·4	40	3·8
12·5 to 12·9	83	7·9
13·0 to 13·4	188	17·9
13·5 to 13·9	215	20·5
14·0 to 14·4	195	18·7
14·5 to 14·9	162	15·4
15·0 to 15·4	88	8·4
15·5 to 15·9	36	3·4
16·0 to 16·4	24	2·3
16·5 to 16·9	4	0·4
17·0 to 17·4	3	0·3
17·5 to 17·9	0	0·0

Summary.

1. Hæmoglobin values were determined on 1265 children who attended schools in Bunbury, Western Australia. This was done by means of the alkaline hæmatin method and an "Eel" photoelectric colorimeter. An inorganic standard described by Gibson and Harrison was also used.

2. The mean hæmoglobin levels were as follows: (*a*) 1265 children aged five to sixteen years, *14·1 grammes per centum*; (*b*) 1049 children aged five to thirteen years, *14·0 grammes per centum*.

3. Determinations were made on 68 adults, 50 of whom were voluntary blood donors for the Red Cross Society. The mean hæmoglobin value for males was found to be 15·9 grammes *per centum* and for females 14·3 grammes *per centum*.

4. These values are considered to be entirely satisfactory and in agreement with standards of normality in Great Britain. They are compared with those of other workers in the light of the British Standards Institution colour standard value of 14·8 grammes *per centum* = 100%.

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This paper would not be complete without a record of *appreciation to the many people whose ready* cooperation and assistance enabled the work to be successfully carried out. Thanks are due in particular to Dr. R. Walsh, Director of the Red Cross Blood Transfusion Service, *Sydney; Mr. K. A. Wright, National Standards Laboratory,* Commonwealth Scientific and Industrial Research Organization, Sydney; Mr. F. R. Barrett, School of Public

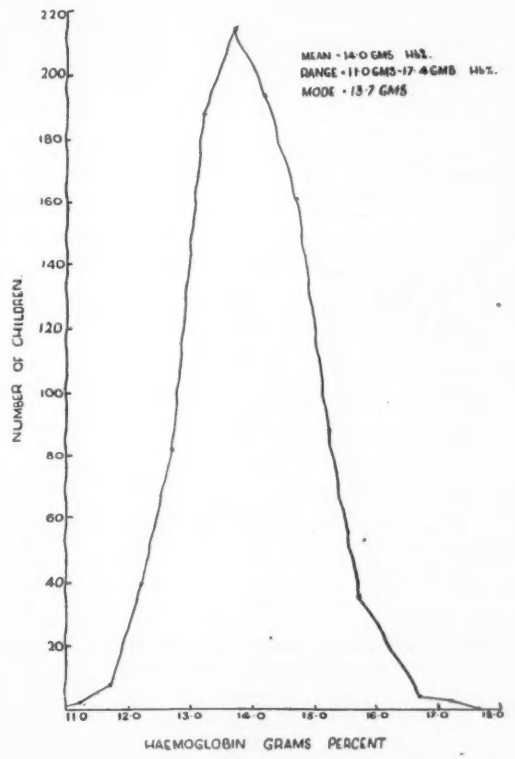

FIGURE I.

Frequency distribution of *hæmoglobin levels for children* aged five to thirteen years inclusive. Curve drawn from data in Table IV.

Health and Tropical Medicine, Sydney; the heads and staffs of the ten schools visited, the doctors who showed an interest in the work, the matrons of the district hospitals.

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THROMBOCYTOPENIC PURPURA IN THE NEW-BORN, WITH REPORT OF A CASE.

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THROMBOCYTOPENIC PURPURA of the new-born is a rare disease. In the majority of reported cases the mother had suffered at some period of her life from the same disease.

Mosher (1923) reported a case of purpura in pregnancy, in which the woman gave birth to a baby girl weighing six and a half pounds, who lived two hours. Wherever the child was touched large ecchymotic spots appeared.

Waltner (1924) reported a case of purpura in the new-born, the child recovering spontaneously. The platelet count was 90,000 per cubic millimetre on the fifth day and the mother suffered from Werlhoff disease before and during pregnancy.

Liebling's patient (1926) suffered from *purpura hæmorrhagica* complicating pregnancy and the child was affected, its platelets numbering 40,000 per cubic millimetre on the fourth day. Both mother and child recovered.

Leschke and Wittkower (1925) reported an example of purpura in the new-born with hæmaturia and melæna. The mother had purpura and her platelets numbered 60,000 per cubic millimetre. The child recovered.

Rodecurt (1928) published an interesting case of universal purpura in a new-born female infant; the platelet count was 127,682 per cubic millimetre and the calcium content of the serum 5·14 milligrammes per 100 cubic centimetres. The child recovered. The mother had excessive post-partum bleeding and her platelets numbered 90,983 per cubic millimetre, but there was no purpura or history of purpura.

In 1929 Greenwald and Sherman published an interesting case of congenital essential thrombocytopenia. A male infant, whose blood contained 30,000 platelets per cubic millimetre, developed purpura first on the sixth day; blood oozed from the circumcized area and from the rectum on the fourteenth day. When the child died, post-mortem examination revealed a congenital anomaly of the heart and the thymus gland consisted mostly of fat tissue which enclosed a few lobules of thymic parenchyma without a single Hassall's corpuscle. Megakaryocytes were scanty in the bone marrow. The mother's blood was not examined.

Bayer (1931) collected four cases, two of these being in twins. The mother's platelet counts were not noted.

Guttfreund (1933), in a long, interesting study of the condition, reported an instance of purpura in a male child aged fourteen days. No platelets at all could be found in his blood. For four months hæmorrhage continued in the child, who then died of pneumonia. The father gave a history of easy bruising and epistaxis and of prolonged bleeding after tooth extraction. The mother's blood platelets numbered only 32,000 per cubic millimetre, but she was symptom-free.

Sanford, Leslie and Crane (1936) reported the case of a female child who at birth was covered with purpuric spots, which deepened in colour until the third day and then faded. The mother had a low platelet count and said that both she and her mother frequently had a similar rash.

Davidson (1937) reported the case of an infant born with the classical features of thrombocytopenic purpura, whose blood contained 56,000 platelets per cubic millimetre and whose mother had been under observation since the age of eleven years and had undergone splenectomy for thrombocytopenic purpura. The child completely recovered and the platelet count was normal at two and a half months. The mother's platelet counts had varied from 6000 to 47,000 per cubic millimetre for many years prior to parturition and did not rise above 21,000 per cubic millimetre for two and a half years after the child's birth.

The generalized purpura in the baby reported by Posner (1937) may have been allergic in origin, as the mother had purpura believed due to allergy to quinine, with a low platelet count. The child recovered.

Whitney and Barrett (1942) reported two fatal cases of thrombocytopenic purpura in the new-born, the children being the offspring of a woman who had undergone splenectomy for thrombocytopenic purpura at the age of fourteen years.

Urbanski and Hutner's patient (1942), a female with thrombocytopenic purpura, had a stillborn male child with generalized petechial hæmorrhages. Later she underwent splenectomy and twenty months later became pregnant. She gave birth to a full-term living female infant with petechiæ on the face, the buccal mucous membrane and the soft palate. In the next two pregnancies the babies were normal.

Finn's second case of purpura in pregnancy (1944) presented an interesting history. Splenectomy had been

performed nine years previously. The first child died. The platelets numbered 120,000 per cubic millimetre, and a cephalohæmatoma on the right parietal area and hæmorrhages into the subcutaneous tissues were present. The next pregnancy ended in abortion at three months. The third baby had purpura but no hæmorrhages, the platelet count was 40,000 per cubic millimetre, and examination of the sternal marrow revealed a decrease in megakaryocytes and failure of production of platelets.

In the report by Schefrin and Shechtman (1945) the mother was not affected and there was no family history of purpura. The child was a female, and purpura was noted immediately after birth and the cord bled. Platelets numbered 67,200 per cubic millimetre. In the first count 52 normoblasts per 100 white blood corpuscles were counted, but the mother was Rh-positive. The baby recovered, and at the age of six weeks the platelets numbered 497,000 per cubic millimetre.

In the same year Barclay reported an instance in a new-born infant whose mother did not suffer from the disease. The platelet count was 6000 per cubic millimetre, but spontaneous recovery occurred.

In Morrison and Samwick's case (1945) of congenital thrombocytopenic purpura both the mother and the maternal grandmother showed evidence of purpura with a tendency to low platelet counts. The patient, a male, had purpura eight hours after birth, with a platelet count of 40,000 per cubic millimetre.

The mother of the patient reported by Patterson (1946) had had chronic purpura and thrombocytopenia since the age of four years. The baby recovered.

Waters (1946) reported a case of thrombocytopenic purpura in a new-born infant whose mother was unaffected. The child recovered.

Goldstein (1947) reported an instance in one of full-time dissimilar twins; the boy was covered with petechiæ immediately after delivery. The platelet count was 63,000 per cubic millimetre. The other twin, a female, was normal, but the platelet count was 158,000 per cubic millimetre. The mother's platelet count was 182,000 per cubic millimetre, but there was no history of purpura.

In the same year Talmadge and Berman reported congenital thrombocytopenic purpura occurring as a familial condition in three successive children of a mother who had undergone splenectomy for thrombocytopenic purpura three years before the first pregnancy. In each of the children there was a gradual spontaneous recovery of the blood picture to normal during the first two months of life.

In 1949 McAlenny and Kristan reported six new cases, and Bluestone and Maslow reported the first case in which splenectomy was performed for essential thrombocytopenic purpura in the new-born infant. The child recovered. There was no history of purpura in the mother.

Report of a Case.

In the case reported here there was no evidence of the condition in the mother, the father or one sibling.

Baby Susan F., a female, whose birth weight was eight pounds two ounces, was well for the first thirty-six hours and no abnormality was noted. On the second day a red area about one inch in diameter was noticed on the baby's back. During the next forty-eight hours bruises appeared on various parts of the body and a fine petechial rash on the forehead; there was also a blood-stained discharge from the left eye. On the fourth day there was a fine petechial rash, most pronounced on the back, but also present over the front of the body, limbs and scalp. Some purpuric spots were also present on the palate. There was no melæna or hæmaturia at any stage. Further physical examination gave negative findings. A blood count at the time when the red area was noticed gave the following information: the hæmoglobin value was 19 grammes *per centum*, and the red corpuscles numbered 6,000,000 per cubic millimetre, the white cells 14,000 per cubic millimetre and the platelets 50,000 per cubic millimetre. The platelets on the stained films were scanty and difficult to find, but no large or aberrant forms were seen.

The infant was sent to the Royal Alexandra Hospital for Children, where a blood count showed that the red cells numbered 5,500,000 per cubic millimetre, the hæmoglobin value was 19 grammes *per centum* and the platelets numbered 110,000 per cubic millimetre. The prothrombin time was normal and the blood group was A, Rh-negative. The baby was given a transfusion of 60 millilitres of blood. Forty-eight hours later the rash had almost disappeared and it was completely gone in the next forty-eight hours, when a blood count showed that the red cells numbered 5,500,000 per cubic millimetre and the platelets 378,000 per cubic millimetre. The infant was well and was discharged from hospital the next day.

The mother, Mrs. F., was aged twenty-five years; she had no history of excessive bleeding or of purpura, and had had no operations and no blood transfusions. She had had one healthy living child, then a miscarriage at four and a half months, then the present baby. Her blood count was normal. Her blood was of group O and Rh-positive. There were no abnormal physical findings and close questioning could not elicit any history of purpura or of hæmorrhage in either her own or her husband's family. Her diet during pregnancy had been satisfactory and her social circumstances were good. Ether was the only anæsthetic used during labour, which was short and without complications.

Discussion.

The differential diagnosis of a case of thrombocytopenic purpura in the new-born may be difficult and quite impossible without laboratory assistance. Leuchæmia in the new-born is a rarity (Smith, 1921; Stransky, 1928; Cooke, 1933; Rhany, 1938; Cross, 1944), but the blood count makes the diagnosis.

In congenital syphilis hæmorrhages occasionally occur from the mucous membranes as well as into the internal organs (Tow, 1937), but other signs and symptoms and the positive reaction to the Wassermann test make the diagnosis.

Multiple hereditary telangiectasia in the neonatal period is extremely rare, but Snyder and Doan (1944) have reported a fatal, homozygous form in which symptoms were present at birth. The platelet count was over 900,000 per cubic millimetre. Hæmorrhagic disease of the new-born due to lack of vitamin *K* may easily cause confusion, as in some cases hæmorrhages may occur into the skin.

Javert (1941) found that the administration of vitamin *K* to pregnant women might prove of little or no value unless the simultaneous use of mineral oid was curtailed.

A most unusual case of hypoprothrombinæmia in the new-born is reported by Sydow (1947). A woman was treated with dicoumarol in the last month of pregnancy. The infant was given vitamin *K* immediately after birth, but a few hours later the skull was covered with subcutaneous hæmorrhages. Repeated daily doses of vitamin *K* did not raise the prothrombin index until six days after birth. In hypoprothrombinæmia the platelet count is normal or high (Morse, 1912).

Hæmolytic disease of the new-born may cause confusion in some cases. Javert (1942) has described erythroblastosis with hæmorrhagic diathesis in three cases, and in one the child had many skin petechiæ. Javert believes that the high incidence of hæmorrhages and skin petechiæ in this condition indicates an unusual capillary permeability. Leonard (1945), in 55 cases of hæmolytic disease of the new-born, found hæmorrhagic manifestations in 16 and petechiæ in 13. These infants had low prothrombin levels and responded poorly to vitamin *K*; this he attributes to impaired liver function.

In infants with hæmolytic disease of the new-born the number of platelets may fall to considerably less than 100,000 per cubic millimetre (Potter, 1947). Pickles (1949) also notes that the blood platelets may be low in number and that the bleeding time may be low and the prothrombin time increased.

Help in diagnosis may be obtained from the serological tests on the mother and child, which should include a Coombs test on the child's cells.

In *asphyxia neonatorum* hæmorrhages may occur. Clifford (1941), in an interesting study of 11 infants suffering from this condition, noted that the majority showed petechial hæmorrhages and subcutaneous ecchymoses, and one vomited blood. He stated that the basic physiological effect of anoxæmia was the production through an accumulation of carbonic and lactic acids of an increased pH in the body. This produces loss of tone and dilatation in the smooth muscle of blood vessels and capillaries, thus allowing the escape of plasma and hæmorrhage.

Dodd and Rapaport (1949) saw amongst the hæmorrhagic manifestations of hypocalcæmia of the neonatal period hæmatemesis, melæna, hæmoptysis and petechiæ of the skin. The patient reported by Bluestone and Maslow (1949) had hypocalcæmia as well as thrombocytopenic purpura, as did Rodecurt's patient (1928). There were several other rare conditions which had to be considered before a diagnosis of thrombocytopenic purpura was made.

According to Miller, Johnson and Durlacher (1944), a tendency to hæmorrhage and other manifestations similar to those in hæmolytic disease are seen in some infants born to diabetic mothers. One of their subjects had skin petechiæ.

Fibrinopenia or even total absence of fibrinogen has been reported several times.

MacFarlane's patient (1938), a boy, had a history of hæmorrhagic tendency from earliest infancy, also thrombocytopenia. Glanzmann's patient (1940) also had thrombocytopenia.

The patient reported by Henderson, Donaldson and Scarborough (1945) had a normal platelet count; but these authors note that a low degree of capillary resistance is also a feature of the disease.

Callahan, Russell and Smith (1946), in a long, interesting article on histoplasmosis, gave full reports of congenital cases of this condition. Hæmorrhage from mouth and rectum, jaundice and purpuric spots were seen in an infant aged three days.

Sepsis in the new-born may cause hæmorrhage and thrombocytopenia.

Beveridge (1928), in a series of 24 cases, found hæmorrhages into the skin in 11. Poncher (1940), in an interesting series of cases of this condition, noted hæmatemesis 16 times, dermal and cutaneous hæmorrhages three times, hæmaturia twice, and melæna eight times.

Grossman (1940) reported petechiæ in 6% of 16 cases of hæmorrhagic disease of the new-born, and in this critical review fully discussed the whole position of vitamin *K* and its importance in the neonatal period. In 1941 he recognized two forms of hæmorrhagic disease of the new-born, clinical and subclinical, the latter being characterized by the occurrence of petechial hæmorrhages on the serous surfaces and mucous membranes of the body; in these cases spontaneous cure occurred, with the usual normal restoration of the prothrombin level by the fourth day.

Brinkhous, Smith and Warner (1937) showed that the prothrombin level in normal new-born babies lay between 14% and 39% of normal, and that in hæmorrhagic disease of the new-born it was less than 5% of normal. Quick and Crossman (1939) showed that the prothrombin level of normal babies six hours old was relatively high and not strikingly different from cord blood, but at the end of twenty-four hours the values dropped to a very low level. After forty-eight hours the concentration began to return to normal, and after three to seven days the values were essentially the same as in adult blood. These findings stress the necessity of not regarding a low prothrombin level as necessarily the cause of hæmorrhages in the neonatal period, and also the rationale of giving vitamin *K* in any hæmorrhagic state in the new-born.

Waddell and Lawson (1940) found a seasonal variation in prothrombin deficiency in the new-born, which was the expression of a lack of vitamin *K* in the diet of pregnant women during the winter season.

Fitzgerald and Webster (1940), in a small series of cases in which sodium phenobarbital was given as an analgesic, found a depression in the prothrombin level of both mother and child.

The question of capillary fragility in the new-born is of great interest, as the vascular factor in hæmostasis has recently come into prominence. The well-known "stork bites" (*nævi pallidi*) and other types of flat, faintly red vascular nævi are common in the new-born and usually disappear spontaneously.

Abt (1936) found uniformly high values for capillary resistance in infants aged under one week. However, he tested six only, and the two youngest were three days old.

Moloney (1943), on the other hand, in a preliminary study of capillary resistance in the new-born, showed that 60% of 55 infants had more or less abnormal capillary fragility which disappeared as the infant grew older. He stressed the fact that the amount and kind of analgesia and anæsthesia, the duration and character of labour and the manner of delivery were factors of paramount importance in the potential production of abnormal fragility in the new-born. He found that the duration of labour in cases in which the infants were affected by severe capillary fragility averaged fourteen hours, and for the "moderate" and "negative" groups five hours. He thought it possible that the analgesic or anæsthetic agents might have a direct effect on the capillary endothelium, but that the end result might be anoxia with the results described by Clifford (1941).

The effect of vitamins on capillary fragility in the new-born merits some discussion, especially the part played by vitamin *C* in the mother's diet.

Dalldorf (1933) believed that the capillary resistance could be used as a criterion of subclinical scurvy. Roberts *et alii* (1937) showed that in children seasonal variations in capillary fragility were pronounced, and found a striking parallelism between the pressure and the level of vitamin *C* supply.

Rapaport (1940) found no correlation between abnormal capillary fragility and *C* avitaminosis. Liebmann (1938) stated that abnormal capillary fragility should be considered as being due to vitamin *C* deficiency only if the vitamin *C* level in the body fluids was low and if the fragility returned to normal after adequate therapy.

Englekes (1935) treated a woman, aged sixty-four years, suffering from essential thrombopenia, with vitamin *C* and obtained good results, even stating that an increase in the number of platelets took place. Williams and Green (1939) obtained temporary improvement with vitamin *C* in a child aged four years, with thrombocytopenic purpura and a deficiency of vitamin *C*. The possible role of vitamin *P* also needs consideration. Jersild (1938) held that vitamin *P* cured the purpura in Schönlein-Henock's disease, and Scarborough (1940) stated that a deficiency of vitamin *P* was invariably associated with much decreased capillary resistance and might be characterized by the development of spontaneous petechial hæmorrhages. Rapaport (1941) considered that vitamin *P* apparently played an important role in the mechanism of permeability of the capillary wall, probably acting as an essential constituent for normal capillary permeability.

Isaacs (1943) found a reduction in hæmorrhagic tendencies, but no changes in the number of platelets, in eight patients with thrombocytopenic purpura after citrus pectin had been taken by mouth.

Kerpel-Fronius *et alii* (1948) have found that capillary fragility in the new-born shows a decided seasonal variation. They note that the higher frequency of cephalhæmatomata and cerebral hæmorrhage in winter and spring seems to be linked with a parallel seasonal variation in capillary fragility and prothrombin deficiency, suggesting a simultaneous deficiency of both vitamin *K* and vitamin *P* in the maternal diet. They suggest giving both vitamin *K* and vitamin *P* during the last months of pregnancy.

The original work on the relation of hæmorrhagic states to vitamin *D* was done by Ivy (1935), and although little notice is now taken of any possible relationship of this vitamin to hæmorrhagic conditions, it is, as Scarborough (1942) states, stimulating to recall the cases of thrombocytopenic purpura reported by Lowenburg and Ginsburg (1936) and by Levine and Michelson (1940).

Ainsworth *et alii* (1937) also reported two interesting cases in children of thrombocytopenic purpura treated with parathyreoid hormone and calcium gluconate, with prompt cessation of purpuric manifestations.

Weld (1936), in some interesting work, concluded that vitamin *D* was a more effective agent than vitamin *C* in increasing capillary resistance. In the case here reported neither the mother nor the child had any clinical evidence of vitamin deficiency, but no laboratory tests were made. The platelet count in the new-born has been studied extensively.

In 1889 Hayem gave the number of platelets on the first day as 171,000 per cubic millimetre, with a gradual rise to 350,000 per cubic millimetre on the eighth or ninth day.

Morse (1912) found the number of platelets at birth to vary greatly, being sometimes high and sometimes low, the low levels rising about the end of the first week and the high levels decreasing during the first few days. On the seventh day the average count was 394,000 per cubic millimetre. Morse found a pronounced increase in *icterus neonatorum*, and in hæmorrhagic disease of the new-born no diminution at the onset, but a post-hæmorrhagic rise with a late maximum.

Slawik (1920) found an average platelet figure of 320,000 per cubic millimetre on the tenth day, one as low as 65,000 per cubic millimetre on the first day.

Lucas *et alii* (1921) gave figures covering the platelet counts from the first to the eighth day, the lowest figure being 196,000 per cubic millimetre and the highest 396,000 per cubic millimetre.

Lippmann (1934) counted the platelets of infants aged from half an hour to forty-eight hours and found that at birth the count was highest, the average being 213,000 per cubic millimetre; during the next six hours there was a sudden drop followed by a slower decrease until eighteen hours after birth, after which there was a tendency to a slow increase. Both Lippmann and Slawik noted that the platelets in the new-born were often larger than in adults and that the variations in size were more pronounced, also variations in the staining properties.

McLean and Caffey (1925) found an average platelet count of 278,000 per cubic millimetre up to five days. The lowest was 216,000 per cubic millimetre. Eckerström (1930), in 46 infants in the first week of life, found the number of platelets to vary between 180,000 and 250,000 per cubic millimetre. Benhamou and Nouchy (1932) believed this variation to be too great. Merritt and Davidson (1933) found a mean value at birth of 227,000 per cubic millimetre, with a gradual rise to 348,000 per cubic millimetre at the third month.

There are no Australian figures.

It is easy to understand that a disturbance in the equilibrium between the factors governing platelet levels and capillary fragility in the new-born can easily cause thrombocytopenic purpura, and that this disturbance is usually mild and transitory is suggested by the comparatively benign course of the disease in many cases in which the mother has not suffered from purpura prior to or during pregnancy.

Bayer (1931) regards the state of the walls of the blood vessels as of great importance.

When the mother has been affected by the disease, the question is different, as transplacental transmission of toxins or platelet-inhibiting substances or hormones has to be considered.

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SOME ASPECTS OF ALLERGY.[1]

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IN this paper it is intended to discuss certain aspects of the study of allergy, and whilst certain conditions of the allergic state will be covered, it is not intended to go into the theoretical considerations which form the basis of the study.

As every one of you is well aware, certain conditions such as hay fever, asthma and urticaria are those which are certainly due to an allergic state; it is becoming increasingly obvious that many conditions are being considered to be due to an allergic cause. Amongst these are *periarteritis nodosa*, Löffler's pneumonia, and even rheumatic fever. However, certain conditions which are considered allergic by ardent allergists and others are to my mind very doubtful; I refer to enuresis in children (*per se*, and not associated with other allergic symptoms) and acute nephritis. The only reference I can find to the latter in respect of supporting evidence that it may be due to an allergic state is the work done by Masugi; he injected a nephrotoxic serum (nephrotoxin) produced by sensitizing ducks to rabbits, and injected this into rabbits, diffuse glomerulonephritis resulting. Aschoff, in discussing this work, considered that the toxin was strong enough to cause damage without any actual sensitization. Whilst we are discussing the question of allergy generally, it is interesting to bring to light two points which so far have not been published regarding the history of allergy. The first of these was that amongst the few reasons for granting a divorce allowed by the mediæval church, one was the occurrence of asthma or hay fever, or both, and dermatitis sufficiently severe to cause prostration, only when the sufferer was in contact with or close to the other partner. The other point of interest is that Samuel Pepys suffered from asthma *et cetera*, which was apparently brought on by heat and cold. It is well described in Arthur Bryant's biography, "Samuel Pepys: The Man in the Making" (1949):

> Every summer he became exceedingly hot and broke out in prickling and itchings all over his arms, breast, thighs and legs: in the winter on the other hand, on the least taking of cold, his nose swelled, his water stopped, and he suffered from an agony of suppressed wind.

Before I conclude this introductory section I must explain with regret that, owing to shortness of time allowed for the preparation of this paper, no statistics or graphs will be shown, as certain statements will be made with which no doubt absolute agreement will not be reached by the listeners. It is desired to pay a tribute here to Dr. H. G. Breidahl, as it was he who directed me along the paths of allergy.

INCIDENCE.

It is well known that a large number of the population have some form or other of allergy, and it is not surprising that eminent workers have found that 6% to 10% of the population suffer from the major forms of allergy—asthma, hay fever *et cetera*—and up to 50% have allergies in either a major or a minor form. The minor form is of the type of single sensitivity, such as that to shellfish or strawberries. This minor allergy may never be repeated.

Another well-known fact is the family incidence of allergic diseases, and the possibility that children may display allergic conditions has been worked out rather fully. According to Urbach and Gottlieb in their book "Allergy" (1947), if one side of the family shows the allergic diathesis, then 33% of the children will suffer from a form of allergy, but if both sides of the family show this diathesis, then 80% of the children will suffer from some form of allergy. I have myself been able to trace a family history through four generations.

[1] Read at a meeting of the Western Australian Branch of the British Medical Association on May 17, 1950.

It is believed that the allergic diathesis is carried by an abnormal or allergenic gene, but beyond that investigations are not much further advanced. The incidence of a positive family history in allergies is in the region of 50% to 75% of cases, and it must be borne in mind that a number of people give no history of allergic manifestations at all simply because they have not been exposed to any sensitizing substances. Vaughan makes mention of a pair of twins exposed to diphtheria—one twin had urticaria and the other had no allergic symptoms. The physician gave antitoxin prophylactically to the twin without symptoms, who promptly died of anaphylactic shock.

One should bear in mind that the allergic manifestation will bear no definite relation to the manifestation present in the previous generation. Thus one finds that the parents may suffer from migraine and grandparents from asthma, but the children will suffer from eczema or seasonal hay fever, or one will find the whole series of conditions reversed.

Again, one may see that Shakespeare's seven ages of man have a similar analogy in the allergic state. Thus one sees the baby with eczema, which clears around the age of two years and is followed by a period of quiescence until the age of six or seven years, when the same child develops mild attacks of asthma, which clear at the age of ten years. At eleven years he develops seasonal hay fever, which at twenty years develops into perennial rhinitis; this may stay with him until he reaches the ripe old age of three score years and ten, at which time he may develop asthma once again. This may be an extreme case, but there are quite a number of similar experiences.

With regard to the incidence of psychopaths amongst allergics, it is considered that the incidence is not any higher than it is in the normal run of the population. This may be regarded as rather sweeping, but the clinics at both the Royal Perth Hospital and the Princess Margaret Hospital have borne out this statement. It will be referred to again when we mention ætiology and symptoms, particularly with regard to asthmatics.

ÆTIOLOGY.

As has been said before, the factor that is carried in each allergic person is the diathesis, which may make itself prominent in a number of different ways, either singly or in a multiple fashion; these multiple manifestations may be evident only at different ages. An example of this is presented by a patient of mine, who suffers from asthma and migraine concurrently.

It is considered that in any discussion on allergy it must be laid down that the ultimate and fundamental basis is the allergic state, and whilst it must be (and is) admitted that other factors are often important, it is the allergic state of the body upon which all the others operate. Such other factors may be: (i) psychological factors, (ii) infection, (iii) climatic conditions, and (iv) endocrine upsets. I now propose to speak of these additional factors and their relation to allergy as a whole.

Psychological Factors.

As was said before, it is not considered that the proportion of psychopathological cases among allergics is any higher than among the rest of the population, but it has been found that any emotional conflict will aggravate the already present allergic condition, although it will not initiate such a condition.

It is customary to quote cases in which a family quarrel has precipitated an attack of asthma in a young child; but in a large proportion of cases careful examination will reveal that it is the prodromal symptoms which make the patient miserable and irritable and which cause the family upset. This will be referred to in the section on diagnosis.

Infection.

Whilst it is admitted that infection will cause an allergic condition to come to light or cause it to be prolonged, it is not considered that infection will give rise to the allergic condition *per se* without the underlying allergic diathesis or established allergic condition.

I had an uncomfortable experience at Christmas, 1949, when I had a small carbuncle on my neck, and every time during the existence of the carbuncle I drank draught beer only, I developed an urticarial rash of the face and neck. Thus the removal of infected tonsils or treatment of a grossly infected sinus may in some cases produce great improvement; in others the results are not so successful.

Climatic Conditions.

There is frequently a profound reaction to climatic disturbances in all forms of allergy, even including migraine of allergic origin. The history given is usually that the condition becomes worse with a fall in the temperature or increase in humidity. Though this on the surface would appear to be purely due to an inhalational factor, it is not borne out by the subsequent history, as frequently we find that the true allergens are foods, but they may show up only with these climatic changes.

In a certain group of cases, as you all know, the allergy lights up only with change of the season, particularly spring and autumn, and in these cases also it may be due to foods. One must always be on the lookout also for those who are allergic to heat and cold. In addition one finds those cases in which the particular allergic condition comes to light only in certain parts of the country and removal to another part brings relief. These forms may be due to foods or to inhalation factors. They are not so common as it is believed, and in fact it is extremely hazardous to recommend change of climate, because the expected relief may not be forthcoming. Dr. H. G. Breidahl has a patient who, whilst she is near the sea, reacts strongly to beans, but when in the wheat belt she does not react to them.

Endocrine Disturbances.

With endocrine disturbances allergy is found mainly in women and mostly around the menopause. It is found that exacerbations of the allergic condition run in a definite rhythm with the menstrual cycle, whether it is regular or not. If an investigation is carried out, it is usually found that the allergy may be due to upset of the endocrine balance, and if this is adjusted relief of the allergic condition will result.

Apart from this, however, allergic manifestations are found which must be regarded as due to endocrine secretions. This subject is well covered by Zondek and Bromberg (1947).

A patient complained that since her menstrual periods had became irregular at the age of forty-five years, she had suffered from nasal obstruction, and had developed a rash over the butterfly area around the nose, which resembled *lupus erythematosus*. These abnormalities were present all the time, but were worse when the menstrual flow began. She was given œstrogen therapy and an injection of one millilitre of "Antuitrin S". However, this was followed by an immense local reaction, which subsided, so it was decided to desensitize her with "Antuitrin S". This was done by commencing with a dose of 0·001 millilitre and gradually increasing it up to one millilitre. At the completion of the desensitization her nasal obstruction had practically cleared and the rash had faded.

It is also found that allergic symptoms are either absent or much less severe during pregnancy. On the other hand, towards the end of pregnancy allergic symptoms may be aggravated. An example of this is intermittent rhinitis; this becomes a practically continuous condition, resulting in nasal obstruction from mucosal congestion, which is only with difficulty relieved by routine treatment.

It is realized that these statements are contentious, and it is regretted that no graphs or statistics are available in their support. It is hoped that they will be received in the spirit of being at present pure opinions, and it is hoped to produce supporting evidence later. Before I leave this factor, it is interesting that Urbach (1944) postulated an endocrine allergenic mechanism in the production of rheumatoid arthritis associated with endocrine dysfunction.

DIAGNOSIS.

In this section it is not intended to present the points of diagnosis of each allergic condition, because you are

already familiar with them; rather, it is intended to bring to your notice certain points which have been matters of interest and wonder as far as I am concerned, and I am sure they are of interest to you. The first point is this: that there is a resemblance in the onset of the condition in many cases of asthma, episodic rhinitis and migraine. The resemblance is that in all forms one finds that many patients state how well they have felt for a varying period before the onset of symptoms. This is followed by a prodromal period and a feeling of irritability, malaise and general lack of that feeling of well-being. This period in its turn is followed by the production of the characteristic symptoms. The prodromal period is the one that has been mentioned before, in which a patient is often stated to have had an attack of asthma following a family quarrel; but in reality the reason for the quarrel is that the patient is in this prodromal period, when his general well-being is "all at sea". In this progression from a feeling of well-being to the prodromal period a resemblance is seen to the hypersensitive state found immediately before the production of anaphylactic shock. Whether the production of the characteristic symptoms is a minor form of anaphylactic shock is something to be considered.

The second point is that made before—that the allergic state is a general condition, no matter what the form in which it expresses itself, and accordingly it is the whole of the respiratory tract that is concerned in attacks affecting both upper and lower portions of the respiratory tract. Thus on one occasion the symptoms and signs in the upper part of the respiratory tract are predominant, whilst on another occasion those in the lower part of the respiratory tract are in the ascendant; but in each case the whole tract is concerned, and associated skin lesions may be present at certain times.

If this is borne in mind, it is interesting to reflect on the association of many so-called "colds" by which attacks of asthma are often preceded. In taking a history one is struck by the fact that these colds do not progress like normal epidemic colds—they do not proceed to secondary infection, and are really never more than a condition of nasal obstruction with watery rhinorrhœa. Of course it is not intended to say that all are like this and that the epidemic cold does not indicate an attack of asthma. It has been ascertained on occasions that no possibility of epidemic coryza has been present, and careful questioning has revealed without doubt that the number of attacks of asthma following epidemic colds is usually small.

In connexion with the study of migraine, it is interesting that Goltman (1936) was able, by investigating a patient who was subjected to craniotomy, to confirm the theories about the causation of the stages of migraine. This he did by observing the changes in the pulsation of the dura following the exhibition of various allergens to this patient, who it was known had previously developed migraine on their exhibition.

This is a suitable point at which to discuss the main points in the taking of an allergic history. It is found best to ask about associated allergic conditions after taking the history of the main complaint. Then it is advisable to find the relationship of these conditions to: (*a*) time of day, (*b*) periodicity and duration, (*c*) climatic and weather changes, (*d*) in women, menstrual changes, and (*e*) previous history and food intake. Inquiries should be made about the presence of domestic animals and the type of bedding. The appetite is next and the particular liking for and dislike of various foods. The approximate amounts of the main foods taken, whilst giving an indication of their relative intake, often reveal dislike of and active nausea associated with certain foods which were not revealed before. In skin conditions particularly, the type of trees, shrubs, grasses and vegetables involved should be determined, and if in other allergic conditions they are suspected agents, inquiry should be made about them.

The usual procedure is to follow the history and careful general examination with the performance of skin tests. These are carried out against common inhalants and foods. In Western Australia more emphasis is laid on foods than in other parts of Australia, and the skin testing is carried out by the intradermal method as being more satisfactory than the scratch method.

This use of the intradermal method is the reason why more consistent results are obtained for foods than with the usual methods, which are more of the subdermal type. It is realized that in certain cases skin tests do not produce reactions in cases in which definite sensitivity is shown, but in the majority of cases skin testing is remarkably reliable and has the added advantage of saving not only time, but expense, which would be involved in attempts to find the offending allergens by investigation of diet and environment. The method of the elimination diet is one in which the supporters find that as much as eighteen months is required to reach finality.

With the intradermal method of skin testing the results are known within a few minutes. It is reasonably safe, but some fear of reactions must be entertained. •It can be estimated that in up to 80% of cases useful skin test reports are obtainable.

When one is testing for endocrine allergies it is necessary (*a*) to use organic products and (*b*) to give them by the subdermal method. The results are read after twenty-four hours. The *rationale* is well described by Zondek and Bromberg (1947).

It has been found that foods are by far the commonest causes of allergic conditions. It is not necessary to carry out tests against individual grasses and flowers in ordinary cases, as there is usually a common denominator with each of these which is believed to be a polysaccharide. The only exception to this is in cases of contact allergy in which it is desired to find the actual causative agent. This common denominator is of use in desensitization against grasses and flowers, as desensitization against one variety is sufficient for them all.

TREATMENT.

In Western Australia the treatment of allergic states is both dietetic and by desensitization. In a large number of cases both methods are used, but again in another group diet alone has been satisfactory in clearing up or relieving the severity of symptoms. In a smaller group still desensitization is the method of choice. The choice of method can be made only by reviewing the whole case from the following points of view: (i) age of patient, (ii) past and family history, (iii) patient's approach to the condition, (iv) history of the major and minor allergic manifestations, and (v) living conditions — (*a*) type of house, (*b*) adequacy of food. From this it will be realized that it is difficult to treat the patient if these conditions are not or cannot be fulfilled. The last condition, that of suitable living conditions, at the present time is one of the hardest to fulfil. It is often a waste of time and valuable material to give a desensitization course of house dust and kapok if the patient is living in an old or overcrowded house where nothing on earth can relieve the constant spreading of dust about the place. The best that can be done is to hope that through the course of desensitization one may be able to diminish the frequency and severity of attacks.

It is for this reason that my object is to treat allergic patients by diet mainly, and so far the results have on the whole been successful. In some cases a "booster" desensitization dose has helped. This is so in the cases of contact dermatitis and pollen dermatitis, in which patients being taken off cereals in all forms have improved on this *régime*; the conditions clear up faster if a course of desensitization is given, and this should be done.

I have gained the impression that certain inhalants act purely as irritants on an already sensitive allergic site and are not true allergens.

These, as I have previously mentioned, are purely personal opinions, but it is certain that when figures are produced they will be amply substantiated.

It is not intended to go into the treatment of the acute allergic attack as exemplified by acute asthma, as this has already been dealt with by other writers—for example, Sutherland (1946) and Halpin (1949).

When formulating a diet it is necessary to try to avoid those things to which it is thought the patient is sensitive, and also at the same time to give the patient an adequate diet. Occasionally the substances to which the patient is sensitive are not those to which he has given reactions in

the skin tests, and one has to forage around, investigating the possibilities, like Sherlock Holmes investigating the "Scandal in Bohemia", until it is found to what the patient is sensitive. Often it is necessary to ask the patient or the patient's parents to prepare a day-to-day account of what has been eaten and what the reactions have been.

It is necessary to keep on a diet which has been found satisfactory for up to two years. The addition one by one of the substances to which the patient was sensitive can then be done, a careful watch being kept for any untoward reactions.

Sometimes it is found that after going on for a long period the patient has a recurrence of his old condition or another new allergic manifestation, and then it is found that the patient has put on "new raiment"—in other words, he has developed new sensitivities. Then the whole of the dieting has to be gone through again. It is the hope of the allergists of this State that if patients are treated satisfactorily in the early stages and at early ages they will be free from the other manifestations which develop later on in life—that is, by treating allergic rhinitis in childhood we shall prevent asthma later on. The period is not yet long enough to determine if this is satisfactory, but it is the opinion of Ratner (1947) in his article on the management of the asthmatic child.

Adjuvant Forms of Treatment.

Antihistamine Drugs.

The antihistamine drugs were developed in both the United States of America and in France from 1937 to 1944. The principal workers in France were Bovet and Halpern. Credit for this work and for the development of "Neoantigern" ("Anthisan" and "Antistine") and of "Benadryl" is due to them in the first place. Those just mentioned are the principal antihistamine drugs used in this state. They are used in urticaria, serum sickness, drug allergy and hay fever. In allergic dermatitis and asthma the results are very disappointing, and in one case when "Benadryl" was prescribed for Parkinsonism, after the patient had just been cleared of dermatitis, extensive dermatitis of the face developed which gradually subsided with the withdrawal of the drug.

The number of antihistamine drugs on the market is legion, and all these are derivatives of the chemical formula which is exemplified in "Benadryl" as a-methylamino ethylbenzhydryl ether hydrochloride.

Unfortunately every one of these drugs has the tendency to cause somnolence, dryness of the mouth, dizziness and nausea. These effects vary with the various drugs and with different patients. The drug which I have found to be most satisfactory from lack of side effects is "Neohetramine", which is produced by John Wyeth, Incorporated; but unfortunately it is not available for sale in Australia, owing to the dollar position. It appears to be more satisfactory in its action on the same conditions than all the others through this lack of side effects.

Iodides.

In cases of asthma in elderly patients, massive doses of iodides (up to 30 grains three times a day) are often beneficial in relieving the frequency of attacks and the amount of sputum that accompanies them. Iodide therapy is often combined with stramonium (up to 15 minims of the tincture) and "Diuretin" (up to 15 grains) with increased relief. In cases of iodide sensitivity ammonium carbonate may be substituted.

Aminophylline, Theophylline, Ethylenediamine.

Aminophylline, theophylline and ethylenediamine may be given (i) in tablets for oral use, in a dose per tablet of 1·5 grains, (ii) in supositories containing 7·0 grains, (iii) in solution for both intramuscular and intravenous injection.

It is found that the use of suppositories ("Cardophylin") may give the greatest relief in asthma. Occasionally suppositories give rise to diarrhœa, and then tablets for anal use should be employed.

Non-Adrenaline Drugs.

The most popular proprietary non-adrenaline drugs are "Isuprel" and "Neoepinine". These are supplied in tablets for sublingual administration ("Neoepinine" 20 milligrammes, "Isuprel" 10 milligrammes). These relieve asthma remarkably well, but occasionally give rise to a feeling of substernal compression and tightness of the chest resembling amyl nitrite, and it is found necessary to reduce the dosage and to give the drug more frequently.

Ephedrine.

Ephedrine is so time-honoured in the relief of hay fever and asthma as to need no more than a passing reference. Indeed, despite the occasional idiosyncrasy to it, it is still preeminent in alleviating attacks of hay fever, despite the introduction of antihistamine drugs. Apart from the idiosyncrasy shown by palpitation which some people exhibit after taking the drug, there are two others which are not often mentioned. These are (*a*) insomnia and (*b*) frequency of micturition. The first may occur even when ephedrine is combined with phenobarbitone. These complications have to be kept in mind if ephedrine is used in the treatment of nocturnal enuresis of infants.

"Neo-Synephrine."

"Neo-Synephrine" is a useful drug which may be employed as an alternative to ephedrine or nasal drops and also for eyelids in allergic conditions of the conjunctivæ. The usual strength for nasal drops is 0·07% of the hydrochloride and for eye drops 0·08% of the hydrochloride. Often obstinate allergic nasal obstruction will respond to "Neo-Synephrine" and not to anything else.

Comment.

There are many other drugs which are useful in all forms of the allergic states, but those presented have been found most effective. The treatment of the acute allergic state, particularly asthma, has been only touched on, but references have been given. It will be realized that all the adjuvant drugs give purely symptomatic relief.

Summary.

It will be realized that unfortunately no supporting evidence has been produced for many of the statements made. This is greatly regretted and it is hoped to repair this omission later.

It must be realized that at present allergy as a specialty is only twenty-five years old and that, although there are a great number of theories as to the causation of allergic conditions, none of them are completely satisfactory, nor do they cover the whole practice. It may be said that allergy is at the stage now that tuberculosis was before Koch discovered the tubercle bacillus. It is therefore not surprising that the path of allergic treatment is not a bed of roses and that failures do occur. However, the various lines of treatment are all raising the standard of therapy and the number of satisfactory cures, and as new developments come forward so will improvements be made.

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Notes on Books, Current Journals and New Appliances.

SCIENTIFIC STUDIES AND THE COLONIAL MEDICAL SERVICE.

THE title of the Colonial Office publication "A Note on Some of the Scientific Studies Undertaken by Members of the Colonial Medical Service during the Period 1930-47, with a Bibliography" is self-explanatory.[1] The bibliography, which makes up more than half the pamphlet, consists of some 1200 to 1300 references from a wide variety of sources. The "note" itself contains brief reference to the subject matter of many individual papers and reports. The subjects referred to include nutrition and deficiency diseases, malaria, trypanosomiasis and tsetse flies, plague, tuberculosis, leprosy, yellow fever, rabies, typhus, helminthology, hæmatology, blackwater fever, neurology and psychiatry, pathology and miscellaneous subjects. The publication is an interesting record of useful work done often under difficult conditions by field workers and will bring to the notice of those interested in particular subjects reports which might otherwise be overlooked.

CHEMOTHERAPY OF LEUCHÆMIA AND LEUCOSARCOMA.

"CHEMOTHERAPY OF LEUKEMIA AND LEUKOSARCOMA" is a report of an exhibit presented at the American Medical Association Convention in June, 1949, by William Dameshek and a group of colleagues.[2] Apart from the title page, preface and bibliography, it is made up of 53 separate sheets of heavy paper, printed on one side only, and assembled in loose-leaf form. Each presents in "show-card" fashion some aspect of the subject, the information being set out in such a way as to be easily grasped on fairly short inspection. The calligraphy and illustrations are of high quality and most attractive. After some consideration of the possible nature and ætiology of leuchæmia and leucosarcoma and their diagnosis, a brief historical outline is given of methods of therapy that have been used. Then the nitrogen mustards, the folic acid antagonists and urethane are dealt with in detail, and a summing up of chemotherapy is made together with a comparison of X-ray therapy and chemotherapy. Dameshek and his colleagues have packed a surprising amount of information into this book, which should be of considerable teaching value just as it stands.

AN INDEX TO SOVIET MEDICAL LITERATURE.

THE intention of the "English Index to Soviet Medical Literature Available in London Libraries" is "to make all those interested in the regular exchange of medical information between countries cognizant of the stream of serious contributions emanating from the U.S.S.R.".[3] If adequate financial support is obtained, it is proposed to issue further volumes at intervals which will provide a continuous index of articles in the standard Russian journals. The present index is not a complete survey of all Soviet medical publications, but an English guide to those journals which are available in London. It also omits certain volumes of journals fully indexed in the "Index Medicus". The present volume covers the years 1945-1947. The next volume, which is planned for issue late in 1950, will cover 1948-1949, and it is hoped to include additional journals from 1945-1949. Thereafter the intention is to issue a volume annually so long as the need remains.

[1] "A Note on Some of the Scientific Studies Undertaken by Members of the Colonial Medical Service during the Period 1939-47, with a Bibliography"; Colonial Number 252; 1949. London: His Majesty's Stationery Office. 9¾" × 6", pp. 48. Price: 1s.

[2] "Chemotherapy of Leukemia and Leukosarcoma", by William Dameshek, M.D., *et alii*. New York: Grune and Stratton. Pp. 55, with illustrations. Price: $4.75.

[3] "English Index to Soviet Medical Periodicals Available in London Libraries, Together with a Location List of the Periodicals Indexed", by Donovan T. Richnell, B.A., F.L.A.; Volume I: 1945-1947; 1950. London: H. K. Lewis and Company, Limited. 11" × 8", pp. 108. Price: 20s.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Allah Laughed", by C. E. G. Beveridge; 1950. Melbourne: The National Press Proprietary, Limited. 7¼" × 5", pp. 268, with many illustrations.

Records the experiences of life in the Sudan for twenty-one years.

"Foot Mechanics: For Chiropodists and Students", by Leslie R. Smart, S.R.N., M.Ch.S., with a foreword by Neville Taylor, M.Ch., F.R.C.S. (England); 1950. London: Baillière, Tindall and Cox. 7¼" × 4¾", pp. 122, with illustrations. Price: 6s.

Covers diagnosis, abnormalities and orthopædic surgery, X rays and clinical photography, physiotherapy and systems of foot correction.

"Practical Post-Mortem Technique: A Handbook for the Student Post-Mortem Technician", by Edwin G. Poynter, R.M.P., S.E.A.N., edited by Louis L. Griffiths, M.A., M.D., B.Ch., B.A.O., D.P.H., with a foreword by John F. Hackwood, M.D., F.R.C.S., F.R.C.S.(E.); 1950. London: Henry Kimpton. 6¾" × 4¼", pp. 134, with 43 illustrations. Price: 9s.

Explains the details of carrying out a post-mortem examination from the technician's viewpoint.

"The Scourge of Rheumatism"; Report of a Conference held by the British Rheumatic Association, London, September, 1949; 1950. London: William Heinemann (Medical Books), Limited. 7" × 4¾", pp. 92. Price: 5s.

Deals with the treatment of rheumatoid arthritis, the care of the rural patient and assistance offered in Britain in the training and employment of the rheumatic handicapped person.

"Manual of Rheumatic Diseases", by W. Paul Holbrook, M.D., and Donald F. Hill, M.D., with the assistance of Charles A. L. Stephens, junior, M.D.; 1950. Chicago: The Year Book Publishers, Incorporated. 8" × 5¼", pp. 182, with 119 illustrations. Price: $4.25.

An attempt to simplify and condense practical information on the diagnosis and treatment of rheumatic diseases.

"Office Treatment of the Nose, Throat and Ear", by Abraham R. Hollender, M.Sc., M.D., F.A.C.S.; Third Edition; 1950. Chicago: The Year Book Publishers, Incorporated. 8" × 5¼", pp. 620, with many illustrations. Price: $7.50.

Covers the management of ear, nose and throat conditions outside hospital wards and the operating theatre.

"Principles of Ophthalmology", by Thomson Henderson, M.D.; 1950. London: William Heinemann (Medical Books), Limited. 8¼" × 5¼", pp. 236, with 63 illustrations. Price: 20s.

Sets out to demonstrate that, despite apparent anomalies, ophthalmological principles are not *sui generis*, but are merely general biological principles applied to and co-ordinated with local anatomical features.

"Practical Hæmatology", by J. V. Dacie, M.B., B.S. (London), M.R.C.P. (London); 1950. London: J. and A. Churchill, Limited. 8½" × 5½", pp. 180, with 13 illustrations. Price: 10s. 6d.

Based on notes prepared for students taking a one-year course for the diploma in clinical pathology.

"Studies in Pathology: Presented to Peter MacCallum", edited by E. S. J. King, T. E. Low and L. B. Cox; 1950. Melbourne: Melbourne University Press. 8½" × 5½", pp. 362, with illustrations. Price: 35s.

Twenty-two papers by students and associates of Professor Peter MacCallum, of the University of Melbourne, collected and presented to him on his sixty-fifth birthday.

"Human Sterilization: Techniques of Permanent Conception Control", by Robert Latou Dickinson, M.D., and Clarence James Gamble, M.D.; 1950. United States of America: Waverly Press, Incorporated. 10" × 7", pp. 40, with illustrations.

Discusses indications for sterilization with methods and results in the male and female subject.

The Medical Journal of Australia

SATURDAY, SEPTEMBER 30, 1950.

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THE AUSTRALIAN PÆDIATRIC ASSOCIATION.

WHEN the pædiatricians of Australia met at the sixth session of the Australasian Medical Congress (British Medical Association) at Perth in August, 1948, they held informal discussions on the establishment of a pædiatric association which would cover every State of the Commonwealth. It was decided that an association should be formed and a provisional committee was appointed; the members were Dr. Lindsay Dey, Professor Lorimer Dods, Dr. H. Boyd Graham and Dr. Robert Southby. The committee met at Melbourne in August, 1949, and arranged for the preparation of a list of foundation members. Dr. Robert Southby agreed to act provisionally as honorary secretary and treasurer and enrolled the foundation members. The Australian Pædiatric Association was inaugurated at Brisbane on May 27, 1950, at Lennon's Hotel after a dinner attended by thirty-eight of the sixty foundation members. In the future this event will, without any doubt, be regarded as an important landmark in the history of Australian pædiatrics.

The objects of the new association are four in number: (*a*) to encourage the study of pædiatrics in Australia; (*b*) to improve the standards of pædiatric practice and stimulate research in pædiatrics; (*c*) to act as a consultant and advisory body on child health; (*d*) to promote personal contact and friendship among pædiatricians at home and abroad. Members are to be elected from among those who specialize in the practice or teaching of pædiatrics, or in pædiatric research, or who are members of the staffs of hospitals caring for children. Members must be pædiatricians of at least five years' standing. Candidates for admission to membership are to be proposed and seconded for membership by members of the Association. The Executive Committee will consider the names of all candidates so proposed and seconded for membership and, at an annual general meeting of members, will nominate for election such candidates as it shall consider desirable. This means that the Executive Committee will act as a kind of scrutinizing or censoring body. The Executive Committee will also have the task of determining how often general meetings of members are to be held, but it is laid down in the rules that at least one such general meeting shall be held each year. At the inaugural meeting Dr. H. Douglas Stephens was elected President, Dr. Lindsay Dey was elected Vice-President and Professor Lorimer Dods was elected Honorary Secretary and Treasurer. Dr. Robert Southby was coopted to complete the Executive Committee. The rules state that, to maintain liaison between each of the States and the Executive Committee, a representative shall be appointed annually for each State not represented on the Executive Committee. The liaison officers appointed at the inaugural meeting were Dr. P. A. Earnshaw, Dr. A. R. Edmonds, Dr. Douglas McKay and Dr. R. Wall.

In his address as President, Dr. H. Douglas Stephens expressed his desire that the Australian Pædiatric Association should be able to speak with authority. He said that it was essential that all States should be represented in the Association and that therefore pædiatricians and those practitioners showing some particular interest in children's ailments should be urged to band together and form a pædiatric society or union in each State. Unless the Australian Pædiatric Association could induce all States to form such societies and enrol every doctor specially interested in the welfare of children, it would not be able to claim that it spoke with authority. He thought that the Association should give a lead to the pædiatric societies and the sections in the several States as to how best to enable pædiatrics to achieve its rightful place in the medical world. It seemed to him desirable that each State should be asked to submit to the next annual meeting a report indicating its activities during the year and offering suggestions for the future.

Members of the medical profession throughout Australia will readily understand the desire of pædiatricians to have some central rallying point for the study of their special branch of medicine, some point from which suggestions might emanate for improvement in the teaching of pædiatrics to medical students and in the training of nurses in the care of children. It is natural, too, that they should wish to have an organization which could act as a consultant and advisory body on child health. There are many who will regret that the new association was not formed as a Special Group within the set-up of the British Medical Association. It is possible that even yet wiser counsels may prevail and that the Australian Pædiatric Association will follow the example of the Australian Society of Anæsthetists and merge its activities with those of the one body which can speak with one voice for the whole of the medical profession—the British Medical Association. It would be possible to write a long treatise on the fundamental place of pædiatrics in the whole structure of medicine, and there is no doubt that voices will have to be raised if reforms in education and practice are to be brought about. The review of child health activities in Australia, which was published in these columns in the issue of July 8, 1950, showed how large a field has to be covered and also how large the gaps at present are. In the filling of these gaps it is inevitable that discussions will take place with governments and statutory bodies. It is to be hoped that until the Australian

Pædiatric Association identifies itself closely with the British Medical Association, it will see that the latter body undertakes any necessary discussions with extra-professional bodies. In this way one medical voice and not two will be heard. In many voices there is danger of misunderstanding, error and dissension.

Current Comment.

MERCURIAL DIURETICS.

NEARLY thirty years ago the parenterally used mercurial diuretics were introduced into clinical practice, and their value has been firmly established. Intravenous injection is generally recognized as the most effective method of administration, but toxic effects may occur, and this technique is not free from risk. Considerable work has been done on the mechanism of action. John J. Duggan and Robert F. Pitts have recently added to this, and have published two articles based on experimental observations made on dogs.[1] In these they point out that, if it is assumed that the mercurial diuretics act by depressing the distal absorption of sodium in the kidney, there is a limit to this action, when the absorptive system has been completely blocked. Further, they find that in the dog even a moderate reduction in glomerular filtration causes a great reduction in the capacity of the kidney to eliminate water and electrolytes. This is, in their opinion, due to a fall in the filtration rate until absorption in the proximal segment of the kidney may be nearly complete, so that little sodium reaches the distal segment. These findings have some bearing on the mechanism of production of œdema, and on that clinical difficulty, mercurial resistance. However, since theophylline compounds have been combined with organic mercurial salts, the effectiveness of these diuretics has been considerably increased, and it appears as if a higher filtration rate reinforces the specific action of the mercury. The modern preparations used to control œdema are powerful and safe in practice, but when they are used for the relief of œdema in the subjects of chronic congestive failure, the continued use of preparations for intravenous or intramuscular injection has drawbacks for both the doctor and the patient. J. Grossman, R. E. Weston, I. S. Edelman and L. Leiter have published a study of a mercurial diuretic suitable for subcutaneous injection.[2] This is "Thiomerin", which is identical with "Mercuzanthin", a mercury-theophylline combination, except that the theophylline has been replaced by a monothiol, which reduces the toxic action on the heart without affecting the diuretic action. Thirty-three patients with cardiac failure were studied, and no other drugs were given, with the exception of digitalis or quinidine. The results obtained with "Thiomerin" were compared with those following the intravenous and intramuscular injection of "Mercuzanthin", and investigations were carried out on the excretion of water, sodium, chloride, and uric acid by these patients. These latter studies, with consideration of the glomerular filtration rate, showed that "Thiomerin", like other mercurial salts, acts by decreasing the activity of the renal tubules. No troubles were encountered with toxic reactions, and the action of this drug appeared comparable with that of the mercury-theophylline drug administered intravenously or intramuscularly. These observations appear to be well controlled, and to establish a case for the use of suitable drugs of this type, which have the advantage of being safe and comfortable to give by the subcutaneous route.

We may now pass to some clinical observations made on the results of the oral administration of mercurial diuretics. Joseph B. Vander Veer, Thomas W. Clark and David S. Marshall[3] carried out a study of 34 patients with chronic congestive failure, divided into two groups, those who had received standard treatment with mercurial diuretics and those who had not. All of these patients suffered from rapidly recurring œdema, and were ambulatory to a variable degree. With few exceptions, all were under the influence of digitalis, and had been given instructions for maintaining a diet of low sodium content. Laboratory investigations were made as required to keep the renal function under adequate review, and the patients were examined at weekly or fortnightly intervals. The diuretic used was a concentrate of "Mercuzanthin"; it was given in the form of tablets, each corresponding to 0·74 millilitre of the solution used for parenteral administration. Every patient received treatment for a period of at least thirty days. Twenty-seven of them had previously been treated with the preparation designed for parenteral administration, and in 25 of these the need for this form of treatment was largely eliminated. During the period of investigation there was a notable decrease in the number of patients requiring readmission to hospital. No serious toxic symptoms were observed, and the patients naturally preferred the oral method to others. The authors conclude from their study that oral administration of these diuretic drugs has a place in the treatment of chronic congestive failure. This report is in agreement with others based on similar investigations. However, a certain degree of caution is necessary in assessing the results of such clinical observations, particularly on ambulant patients. This caution is all the more necessary when the need for accurate studies of absorption and excretion is considered. In the same journal, William J. Overman, William H. Gordon and G. E. Burch contribute some observations on the urinary excretion of a radioactive tracer preparation of mercury following the oral administration of a mercurial diuretic. They used a mercury-theophylline diuretic of standard form, but prepared with radioactive mercury, and given in the form of capsules. Twenty-two control subjects were used, and five patients with congestive cardiac failure. Single doses of the diuretic were given enclosed in plain and enteric-coated capsules, and by the familiar methods used in detection of radioactive substances, the blood concentrations and urinary excretion of the tracer mercury were determined. In no instance was the urinary excretion after oral dosage comparable with that found after injection, nor did it reach the level of a therapeutic dose. Enteric-coated capsules gave worse results than the plain, indicating that absorption is better from the upper part of the digestive tract. The amount of the drug excreted in the urine was only 5% of that administered orally. Overman, Gordon and Burch conclude that the poor degree of absorption of the preparations for oral use precludes them from being generally used in the treatment of congestive failure. This work suggests that modern investigations with tracer substances are likely to subject our clinical conclusions to more searching review.

[1] *The Journal of Clinical Investigation*, March, 1950.
[2] *Circulation*, April, 1950.
[3] *Ibidem*.

AUREOMYCIN AND AMŒBIASIS.

EVIDENCE so far available indicates that aureomycin is a valuable new aid in the treatment of amœbiasis, particularly the more intractable infections. Of 38 patients with active amœbiasis treated by J. D. Hughes,[1] 27 are regarded as "cured", though the standard of "cure" adopted was not very exacting. Practically all patients treated reported great relief of symptoms, even those whose fæces still contained evidence of the parasite. The dosage, which Hughes points out was more or less arbitrary, was 28 capsules of aureomycin (0·25 gramme) given over a period of four to seven days. Almost all the patients had had repeated ineffective courses of carbarsone, diiodohydroxyquinoline ("Diiodoquin") and iodochlorohydroxy-

[1] *The Journal of the American Medical Association*, April, 1950.

quinoline ("Vioform"). A few had had emetine hydrochloride and chiniofon without being cured. Thus it is clear that the patients most difficult to cure were selected for aureomycin therapy. The criteria of "cure" were abolition of symptoms and absence of evidence of the parasite in five warm liquid stools examined after saline purgation at least two weeks after the last dose of aureomycin. These criteria are not ideal, even though in most cases examination of stools was made at intervals of two to three months and the result remained negative. However, they have some practical significance, and considered in conjunction with the type of infection treated, support the value of aureomycin therapy.

A more recent report provides stricter criteria and the conclusions are qualified though still favourable. T. G. Armstrong, A. J. Wilmot and R. Elsdon-Dew,[1] working in Durban, where amœbiasis is endemic among the native Africans, treated with aureomycin alone 52 patients suffering from acute ulcerative amœbic dysentery, and in the great majority of cases symptoms were quickly relieved, evidence of the presence of amœbæ disappeared and colonic ulcers healed. Their dosage was 0·25 gramme given four times daily at six-hourly intervals for fifteen days. Armstrong, Wilmot and Elsdon-Dew have been engaged for some years in therapeutic trials with the great amount of clinical material at their disposal, and they include in their paper a comparative table of early results from various forms of therapy for acute amœbic dysentery. This shows that aureomycin effected immediate "cure" in a higher proportion of cases than did emetine or any other single drug; but the relapse rate in the first month after cessation of treatment was high. It is clear that the patients' circumstances after they left hospital made reinfection extremely likely, but the more conservative view is adopted and recrudescence assumed to explain reappearance of signs of infection. On this basis it is recommended that aureomycin should not be used alone, but should be combined with some other known amœbicidal agent. Armstrong, Wilmot and Elsdon-Dew think that with aureomycin the dosage of emetine or emetine-bismuth-iodide could be drastically reduced, and, though they have as yet no evidence, they believe that association of "Diiodoquin" with aureomycin would reduce the relapse rate satisfactorily. In their view the great potency of aureomycin suggests its use as the drug of selection in the treatment of acute ulcerative amœbiasis and, though other agents must be used as well, its advent has brought closer the day of ambulant treatment for this disease.

CANCER AND TOBACCO SMOKING.

THE possible association of tobacco smoking and cancer in various forms is not a new idea. It has, however, been viewed with caution, for which at least two reasons immediately suggest themselves: firstly, a wariness of simple and obvious answers to the problem of neoplastic activity, the path of whose investigation is strewn with the like; secondly, fear of the label of "crank" that is readily pinned on any who dare to cast shadows on a popular pleasure. The first reason is sound but not to be overdone; the second is wholly illogical but not without virtue. Neither allows us to overlook two papers on the subject that recently appeared together.[2] In one Ernest L. Wynder and Evarts A. Graham present their investigation into tobacco smoking as a possible ætiological factor in 684 proved cases of bronchiogenic carcinoma. Their work in this is just one phase of a full investigation into various exogenous factors that might play a role in the induction of bronchiogenic carcinoma, so that they are under no suspicion of special antagonism to tobacco as such. Their information was all obtained by personal interview with the patients and has been carefully sifted and analysed with suitable controls. Their conclusion is that excessive and prolonged use of tobacco, especially in the form of cigarettes, seems to be an important factor in the induction of bronchiogenic carcinoma. Among 605 men with bronchiogenic carcinoma, other than adenocarcinoma, 96·5% were moderately heavy to chain smokers for many years, compared with 73·7% among the general male population without cancer; among the cancer group 51·2% were excessive or chain smokers compared to 19·1% in the general hospital group without cancer. The occurrence of carcinoma of the lung in a male non-smoker or minimal smoker is rare—the incidence is 2%. The number of women in the group investigated was rather small and less importance can be attached to the findings; tobacco seems to have been important in the induction of epidermoid and undifferentiated carcinoma of the lungs amongst them, though it is to be noted that the proportion of non-smokers affected is much higher than among men, so far as the wide difference in the size of the two groups permits of valid comparison. It is suggested that one reason for the greater incidence of the disease among men than among women today relates to duration of smoking; 96·1% of patients with cancer of the lungs who had a history of smoking had smoked for over twenty years, and few women have smoked for such a length of time. Another finding of interest is that there may be a lag period of ten years or more between the cessation of tobacco smoking and the occurrence of clinical symptoms of cancer. With regard to the type of smoking involved, 94·1% of male patients with cancer of the lungs were cigarette smokers, 4·0% were pipe smokers and 3·5% were cigar smokers. This prevalence of cigarette smokers is greater than among the general hospital population of the same age group. The habit of inhalation among cigarette smokers may be the significant factor. Adenocarcinoma of the lung is less common than other types of lung cancer and the numbers investigated are small; the figures suggest that tobacco smoking is less important, though still significant, among men, but of no apparent significance among women.

Supporting these findings and also dealing with carcinoma of the lip is a preliminary report in the same journal by Morton L. Levin, Hyman Goldstein and Paul R. Gerhardt. It is based on a study of 1045 male cancer patients and 605 male patients without cancer. The cancer sites selected were lung, lip, pharynx, œsophagus, colon, rectum and a scattered number of other sites. The non-cancer patients were those with symptoms referable to the same sites but not due to cancer. The significant findings are that there were more smokers among cancer patients than among non-cancer patients, because of an excess of cigarette and pipe smokers among the former. This excess was due entirely to the increased percentage of cigarette smokers among patients with cancer of the lung and the increased percentage of pipe smokers among patients with cancer of the lip. These differences, in turn, were confined to those who had smoked cigarettes or pipes for twenty-five years or longer. No other site of cancer included in the study was found to be associated with any particular type of smoking. In summary, the data indicate that, in a hospital population, cancer of the lung occurs more than twice as often among those who have smoked cigarettes for twenty-five years than among other smokers or non-smokers of comparable age; lip cancer bears almost the same relation to pipe smoking of similar duration; cancer in other sites and other forms of smoking are not apparently involved. It is rightly pointed out that these associations do not establish a causal relation between cigarette and pipe smoking and lung and lip cancer respectively. Some other unidentified common factor may be responsible, and it is clear that other factors are concerned, for example, when lung cancer occurs in non-smokers or when heavy smokers are not affected. A good deal needs to be worked out yet. However, the basic findings appear worthy of serious pondering. Bronchiogenic carcinoma is stated to be on the increase amongst men. These data indicate that it is rare amongst non-smokers. It is tempting to suggest that further increase is at least partly preventible.

[1] *The Lancet*, July 1, 1950.

[2] *The Journal of the American Medical Association*, May 27, 1950.

Abstracts from Medical Literature.

THERAPEUTICS.

"Furmethide."

C. NEY AND W. HOROWITZ (*The Journal of the American Medical Association*, January 7, 1950) report two cases of acute pyelonephritis developing as a result of the use of "Furmethide" (furfuryl trimethylammonium iodide) in the treatment of two patients with large amounts of residual urine and vesico-ureteral reflux. One child with *spina bifida* was given "Furmethide", with the result that the amount of residual urine increased, and eventually pyelonephritis developed. The second patient was a man, aged twenty-eight years, who had transverse myelitis. He developed retention of urine and eventually stones in the bladder. These were crushed, and later he again had retention of urine with various complicating factors. He was given "Furmethide" in doses of five milligrammes every eight hours by injection and 10 milligrammes orally one and a half hours after each injection. Pyelonephritis developed. In each of these cases improvement followed at once on discontinuance of "Furmethide" therapy. The authors state that this report is not to be construed as a condemnation of the particular drug "Furmethide", as they believe that any effective parasympathetic-stimulating drug would produce the same complication.

Aureomycin in Influenzal Meningitis.

M. E. DRAKE *et alii* (*The Journal of the American Medical Association*, February 18, 1950) report the results of treatment with aureomycin of seven patients suffering from influenzal meningitis. The results were uniformly successful. The authors discuss the disadvantages of other forms of treatment, and suggest that aureomycin may prove a highly effective and convenient form of therapy in influenzal meningitis.

The Prevention of Pain from Heparin Injection.

M. S. TUCHMAN AND S. E. MOOLTEN (*The American Journal of the Medical Sciences*, February, 1950) state that heparin in doses up to 100 milligrammes can be given subcutaneously and repeatedly with little or no pain to the patient and with rapid effect on the coagulation time if the site of injection is first infiltrated with a small amount of hyaluronidase solution. The procedure is relatively simple and easily carried out by the nursing staff.

The Diuretic Action of "Thiomerin".

C. D. ENSELBERG AND H. G. SIMMONS (*The American Journal of the Medical Sciences*, February, 1950) report their clinical experience with "Thiomerin" in 3314 injections given to 205 patients. Diuretic response to the drug was the same qualitatively, and appeared to be about the same quantitatively, as to the theophylline-containing mercurials. Hypersensitivity reactions and general toxic effects were not met. Local reactions, which sometimes occurred in the early experience, were not met later, presumably because of improved manufacturing methods. The authors regard "Thiomerin", administered subcutaneously, as a safe and efficient diuretic.

Penicillin and Uncomplicated Gonorrhœa.

A. J. KING, F. R. CURTIS AND C. S. NICOL (*The Lancet*, April 15, 1950) treated 2269 patients who had uncomplicated gonorrhœa; all received 150,000 units of sodium penicillin in water, in five doses each of 30,000 units given at intervals of two hours. Of 1879 who attended for tests of cure, 6·4% of men and 3·5% of women experienced immediate failure of treatment; of the remainder, 37·7% of men experienced late failure of treatment ("relapse" or residual infection) and 13·4% of women had the gonococcus in genital secretions two weeks or more after treatment. The authors consider that reinfection does not account for most of these failures and suggest that penicillin is less effective in the treatment of acute uncomplicated gonorrhœa than it is generally reported to be.

Urinary Infections and "Gantrisin".

G. CARROLL, H. N. ALLEN AND H. FLYNN (*The Journal of the American Medical Association*, January 14, 1950) describe a new sulphonamide called "Gantrisin" for use in urinary infections. The full name of "Gantrisin" is 3,4-dimethyl-5-sulphanilamido-isoxazole. It has also been called NV-445. *In vitro* the drug was effective against *Proteus, Alcaligenes, Escherichia coli*, the paracolon bacillus, *Escherichia intermedium, Aerobacter aerogenes, Streptococcus fæcalis* and *Pseudomonas*, in decreasing order of sensitivity. *In vivo* the drug was given in doses of one to two grammes every six hours orally for up to one week. In the presence of nausea or vomiting or inability to take the drug by mouth, it was given intramuscularly or intravenously. Eighty patients with urinary infections were studied; many of the infections were mixed. Against *Proteus, Escherichia coli, Alcaligenes* and certain intermediate organisms "Gantrisin" was the drug of choice. Against *Aerobacter* and the paracolon bacillus it was moderately effective. *Pseudomonas* and *Streptococcus fæcalis* were resistant to "Gantrisin". There were no ill effects, in spite of the fact that alkalis were not given and fluid intake was not forced. The authors consider that "Gantrisin" is the drug of choice in the treatment of urinary infections. In several cases infections resistant to streptomycin responded well to "Gantrisin".

Paroxysmal Supraventricular Tachycardia and Lanatoside C.

J. GORDON BARROW (*Annals of Internal Medicine*, January, 1950) describes the treatment of paroxysmal supraventricular tachycardia with lanatoside *C*, and reports on the results in 26 cases. All cases were diagnosed electrocardiographically, and in all treatment was first tried by carotid sinus and ocular pressure, gagging, and the Valsalva manœuvre. This form of therapy was applied for at least five minutes before lanatoside *C* was injected intravenously. A total dose of usually 1·2 milligrammes of the drug was administered over a period of sixty to one hundred and twenty seconds. If the rhythm did not revert to normal within thirty minutes, a further dose of 0·4 milligramme was given into the vein. A second electrocardiogram was recorded after the abnormal rhythm had ceased. Nausea was the only unpleasant symptom experienced by any of the patients during treatment. In the series of patients presented, there seemed to be no underlying disease which especially predisposed to paroxysmal tachycardia. Attacks which had persisted for long periods of time were more refractory to treatment than the average infection. Toxic symptoms after administration of lanatoside *C* were not observed in any case, only mild nausea being noted in two cases. The arrhythmia was stopped in all cases within one and a half hours. The drug is considered the one of choice in this condition, and safe to administer both in the home and in hospital. Electrocardiographic control is necessary at all times.

Hæmoptysis Treated by Aerosol Administration of Human Thrombin.

J. D. WASSERSUG (*Diseases of the Chest*, March, 1950) describes the treatment of pulmonary hæmorrhage with human thrombin by aerosol administration. In one case described in detail the hæmoptysis was promptly inhibited and there was remarkable control of cough. The treatment did not appear to do any harm to the underlying disease. It is considered inadvisable to use bovine thrombin because of the likelihood of its provoking allergic reactions.

Shock due to Myocardial Infarction.

FRANKLIN H. EPSTEIN AND ARNOLD S. RELMAN (*The New England Journal of Medicine*, December 8, 1949) discuss the result of transfusion treatment of shock due to myocardial infarction, as observed in a series of 30 patients. The clinical observations are compared with the natural history of the disease as noted in a control series of 20 patients not given transfusions. Although transfusion seemed to be of benefit in a few cases, there was no significant difference between the two groups in mortality and recovery from shock. Transfusion did not seem to increase the incidence of pulmonary œdema or the severity of congestive heart failure.

Basal Ganglia.

D. SCIARRA, S. CARTER AND H. H. MERRITT (*The Journal of the American Medical Association*, December 24, 1949) review the effects of caramiphen hydrochloride (panparnit) in the treatment of diseases of the basal ganglia. They state that Parkinson's syndrome has been the subject of many new treatments since in 1882 the use of hyoscine was first advocated. Since then belladonna, atropine, hyoscyamine and scopolamine have been used extensively. Later Bulgarian belladonna root was "boosted", unjustifiably. "Benzedrine" has been recommended to combat somnolence and lethargy in Parkinsonism (a rare event). Vitamin B_6, "Dolantin", curare and "Benadryl" have also been praised, but not enthusiastically. The conclusion is reached that there is no satisfactory drug in the treatment of Parkinson's

syndrome. In the investigation now reported, panparnit was given to 17 patients with post-encephalitic and 11 with arteriosclerotic or idiopathic Parkinsonism without clear benefit. It was tried also without benefit in chronic chorea, *dystonia musculorum deformans*, bilateral athetosis, hepatolenticular degeneration and familial tremors. Toxic effects were giddiness, nausea, anorexia, vomiting, drowsiness and weakness, blurring of vision and diplopia. The general effect appears to have been ineffective and toxic to a degree beyond that usual with drugs employed in these disorders.

NEUROLOGY AND PSYCHIATRY.

Marriage Counselling.

ROBERT W. LAIDLAW (*The American Journal of Psychiatry*, April, 1950) states that marriage counselling is a form of short-timed psychotherapy carried out on the conscious level, dealing with interpersonal relations in which the problems relating to marriage are the centre. It appears that the psychosexual component constitutes the major emphasis in marriage counselling, and assistance should be non-moralizing, helping the patients to work out solutions, dictated by their own needs and circumstances. The premarital period is the most fruitful time for instruction. The patients' factual knowledge is of little avail if attitudes of shame and resistance regarding sex continue to exist. It has been found that matters of sexual technique are of much less importance than the couple's basic attitudes towards sex, and towards each other. The longer marital difficulties have existed before help is sought, the greater as a rule is the therapeutic problem. Lay counsellors can function more effectively in premarital problems and in problems arising shortly after marriage; long-standing problems are well within the field of clinical psychiatry. At times help can be given to ease the impact and lessen the tension of divorce.

Combat Exhaustion.

R. L. SWANK (*The Journal of Nervous and Mental Disease*, June, 1949) discusses findings from upwards of 4000 combat casualties in World War II; the majority of the subjects were American veterans of the Normandy campaign. He draws attention to the relationship of combat exhaustion to the casualty curve. When about 65% of the men are casualties the remainder have a fear of extinction. This becomes an overwhelming incidence. The author pleads for a right attitude towards motivation, and considers that combat exhaustion is lessened if the soldier has the incentive of knowing that he would be out of the line after a stated number of days in combat. Thus on the basis of casualty rates in Italy (about 75% and 100% of the original men were casualties at the end of 125 and 300 days respectively), the headquarters of the army ground forces recommended that this goal (the tour of duty) be one hundred and twenty days. The author considers that the uniformity of the psychological and somatic reactions in soldiers who developed combat exhaustion is worthy of comment. Two mechanisms are responsible: first, to protect itself from an overwhelming threat to its existence, the organism becomes completely and continuously alert, and this leads to severe and continuous emotional tension; second, a constant rapid dissipation of emotional tension leads to emotional fatigue or exhaustion. Few cases of hysteria were recorded. It was noticeable that some men with severe instability prior to entering service remained in combat for long periods, and that many men stable before combat performed poorly in combat.

The Diagnosis of Paraphysial Cysts.

JAMES W. D. BULL AND DAVID SUTTON (*Brain*, December, 1949) discuss the diagnosis of paraphysial cysts. They state that these are also known as colloid cysts, occur in the third ventricle, are usually small in size, rarely exceeding two to three centimetres in diameter, are benign in character, but because of their situation are dangerous to life. They arise from the paraphysis, a glandular structure formed as an evagination from the roof of the third ventricle. They occur in either sex and usually in adults between the ages of twenty and fifty years. There is no clinical characteristic feature. Intermittent symptoms such as headache frequently occur. The diagnosis is made by ventriculography; the authors report that a correct diagnosis was made in 19 cases out of 20. The only useful treatment is surgery.

Test Performances of the Brain Injured and the Brain Diseased.

ROBERT M. ALLEN (*The American Journal of Psychiatry*, September, 1949) reports the results of test performances of the brain injured and the brain diseased. The Bellevue intelligence scale was used for the comparison, and showed similar function losses in both groups in addition to a consistent mean subtest pattern, the information subtest score being used as the basal point of computation of the deviation. The order of deviation of the 10 subtests—from most to least deviated—was as follows: digit symbol, digit span, block design, object assembly, picture arrangement. The author states that the test results indicate that the functioning and efficiency of the patients in both groups follow a similar pattern, verbal scores being significantly higher than performance ratings. The patients with brain injury on the average showed greater discrepancies between the results of the verbal and performance subtests. It is pointed out that the effects of an encephalopathic process are serious, but an immeasurable consideration must be given to the personality structures of the patient, a matter which at present does not lend itself to statistical techniques.

Precocious Puberty and the Hypothalamus.

C. P. J. STOTIJN AND W. J. H. NAUTA (*The Journal of Nervous and Mental Disease*, March, 1950) report the case of a boy who died at the age of ten years and eight months with a tumour of the hypothalamus. They state that at the fourth year abnormal growth occurred, particularly in the genitals. Erections were frequent. Pubic and facial hair developed. About the same time there were bouts of somnolence and later epileptiform attacks. Behaviour was egocentric and asocial. The child was kept in hospital for four years. Post-mortem examination revealed a relatively large tumour in the hypothalamus. The authors review the literature. They state that the site and size of the tumours suggest that there is interference with the blood vessels of the median eminence. The caudal (retroinfundibular) part of the median eminence is especially involved in the transmission of hypothalamic control over gonadotropic functions.

Chronic Disease and an Aging Population.

HOWARD A. RUSK (*The American Journal of Psychiatry*, October, 1949) quotes the increasing extension of the average length of life and states that until the ætiology and treatment for the chronic diseases producing disabilities are found, it can be expected that, as the population ages, the extent of the physical disabilities in the nation will progressively increase. Rehabilitation to the extent of self-care and even full or limited employment is possible for many who have been treated in hospital over long periods. It is recommended that approximately 20% of the beds in general hospitals should be used for this purpose, and that a dynamic rehabilitation programme would reduce hospital days, provide facilities for the evaluating of disabled patients and complete the programme of total medical care. This training should commence at the earliest possible moment and is not complete until satisfactory employment has been found. The aged patient fears isolation, and the majority wish for the opportunity to do something purposeful and constructive; work therapy has been much neglected in this class of patient. Small, standardized, economically built hospitals of 100 bed units are recommended for the senile psychotics. Community day centres for the aged are suggested as a means of lessening dependency and stay in hospital. It is noticed that every advance made in medical science is increasing the number of physically disabled and chronically ill.

Massive Spontaneous Hæmorrhage in Gliomata.

L. O. J. MANGANIELLO (*The Journal of Nervous and Mental Disease*, October, 1949) records seven verified cases of massive spontaneous hæmorrhage in gliomata. Two had a vague relationship with preceding trauma. The cases represent 3·8% of the total gliomata in the author's series. The total duration of symptoms from onset to death was less than a year. The most important finding was the steady progress of symptoms prior to the vascular insult. The author states that the physiological mechanism is similar whether it occurs in normal brain tissue or in gliomatous brain tissue. Sometimes such cases are mistaken for hæmorrhage in the course of a hyperpietic syndrome. The differentiating features are shown by the clinical history. The author considers that the entity of gliomata with massive spontaneous hæmorrhage is sufficiently clear to warrant classification as a clinical entity.

Medical Societies.

THE MEDICAL SCIENCES CLUB OF SOUTH AUSTRALIA.

A MEETING of the Medical Sciences Club of South Australia was held on July 7, 1950, in the Anatomy Lecture Theatre, Frome Road, Adelaide.

Staphylococcal Bacteriophages.

MISS S. MACLEAN read a paper on staphylococcal bacteriophages. She said that many strains of staphylococci were phage carriers and were known as lysogenic strains; the symbiosis between phage and host was very intimate and the host was not lysed. Phage could be obtained from these strains by cross-plating them with suitable susceptible strains. Most of the work on isolation of staphylococcal phages had been carried out with strains of *Staphylococcus aureus* of human origin. In the present study strains of *Staphylococcus aureus* of animal origin, mainly from bovine mastitis, had been investigated. A collection of 36 strains was cross-cultured, 85 lytic combinations were detected, and 45 of the phages were isolated and purified. Cross resistance tests showed that many of the phages were identical, there being only five different phages. In some cases these had been propagated on lysogenic strains and irregular results were obtained due to the presence of contaminating phage from the propagating strain. The typing reactions of three of the phages confirmed the findings of Williams Smith (1948) that apparent differences between strains of staphylococci might be due to acquired phage resistance. Thirty-six strains of *Staphylococcus albus* were also cross-plated, and only one lysogenic culture was detected which carried a phage active on only one strain. This phage had no action on 35 strains of *Staphylococcus albus* or on 70 strains of *Staphylococcus aureus*. Failure to detect more than one lysogenic strain among this group might have been due to the rather heterogeneous nature of the strains, or it might have been due to the fact that some of the strains were mucoid; this might have prevented phage action.

The Adaptation of Bacteria to Antibacterial Substances.

MRS. J. LLEWELLYN said that bacteria possessed the capacity, in varying degrees, to adapt themselves to resist higher concentrations of certain antibacterial substances to which they were initially very susceptible. This increased resistance might be brought about *in vitro* by growing the organisms in broth culture in the presence of progressively increasing concentrations of the drug, and similarly *in vivo* by passaging the organisms through animals just previously treated with subbacteriostatic concentrations of the drug. The development of such drug-resistant organisms had an important clinical significance. Most organisms could become resistant to streptomycin very readily, and resistance to other antibiotics, such as penicillin and the active extract of the mushroom, *Psalliota xanthoderma*, could be induced with moderate ease. However, it was extremely difficult to adapt organisms to resist very slight increases in concentration of protoplasmic poisons, for example, "Monacrin", "Merthiolate" and "Cetavlon". Usually the increased resistance of the organisms was stable, and this evidence, together with the mode of adaptation, suggested that adaptation occurred by mutation, rather than by a direct effect of the drug on the organisms. The effect of two drugs acting simultaneously upon the organisms was greater than either alone, and so far it had been impossible to adapt bacteria to two drugs at the same time, although organisms could be made resistant to two drugs by adapting first to one drug and then to the other. Bacteria with induced drug resistance sometimes showed alterations in specific characteristics, such as morphology, enzymic activity and susceptibility to specific bacteriophage. By cross-titrating resistant organisms with other antibacterial agents, it was possible to determine whether different antibacterial agents acted upon the organisms in the same way.

MELBOURNE PÆDIATRIC SOCIETY.

A MEETING of the Melbourne Pædiatric Society was held at the Children's Hospital, Carlton, Victoria, on July 12, 1950. The meeting took the form of a series of clinical demonstrations by members of the society followed by a paper on pertussis hæmagglutinin.

Xeroderma Pigmentosa.

DR. ARTHUR DAY, in presenting a patient with *xeroderma pigmentosa*, said that usually there was no excuse for merely showing patients as examples of rare diseases unless some useful lesson could be learned. However, it was unusual to have been able to follow a patient with *xeroderma pigmentosa* for so long a period—from the age of four years to twenty-one years. Furthermore, a demonstration of the inevitable unfortunate sequence of events clearly showed the serious prognosis of this disease. *Xeroderma pigmentosa* was directly associated with exposure to sunlight, and the sites of predilection were the exposed surfaces of the body. Kaposi regarded the condition as a congenital debility of the skin whereby exposure to light and air could produce in a few years changes which in a normal skin occurred only after a long life of exposure. The irritation of the actinic rays of light was the exciting factor, but no sensitizing substance, such as hæmatoporphyrin, had been demonstrated. The disease did not appear to be hereditary. The fact that patients rarely survived puberty was the probable explanation. However, Cockayne thought that, with regard to inheritance, *xeroderma pigmentosa* agreed in all respects with a simple recessive character due to a single gene.

Dr. Day said that in some twenty years' association with the dermatological department of the Children's Hospital he had encountered only two cases of *xeroderma pigmentosa*. The disease appeared early in life, the first stage of erythroderma corresponding to the time when the child got out of doors freely; there was mottling, diffuse hyperæmia and some roughening of the surfaces. The second stage of reaction occurred about the age of four years, when pigmentation became more apparent in small freckle-like spots together with active scaling and usually transient flat warts. Hyperæmia of the conjunctivæ became noticeable and was associated with photophobia. The final stage showed characteristic atrophic spots, often with dilated capillaries about the edges and between the pigmented areas, and warty lesions which became more numerous and pronounced. Some of these lesions after months or years became carcinomatous. Erythema, pigmentation, atrophy, and tumour formation were often found side by side. The course of the disease varied in rapidity, but ultimately the lesions became carcinomatous. The whole process was comparable to that of radiodermatitis.

Dr. Day said that his patient, a girl, aged twenty-one years, had shown all these features, and her disease was now well advanced into the third stage. She had first been examined at the age of four years, when there were pigmentation and atrophy of the skin of the face, hands, arms and legs. A diagnosis of *xeroderma pigmentosa* was easily made at this stage. She had a history of having first been brought for attention when aged six months because of irritation about the face and hands, and had then been diagnosed and treated as suffering from infantile eczema. Her mother had used various ointments almost continuously on the advice of a number of doctors, but the lesions had persisted and gradually become worse. Dr. Day commented that it was easy to realize how a diagnosis of infantile eczema could be made in the initial phases of the disease. Since coming to the Children's Hospital at the age of four years the patient had been under constant supervision, but the skin condition had steadily deteriorated, and up to the present she had had six lumps removed, including five epitheliomata and one basal-celled carcinoma, all of which were diagnosed histologically. She now had definite keratitis with much diminution of vision and considerable photophobia. There were extensive skin changes on all exposed parts of the body, the face, hands, arms and legs; erythema, pigmentation, atrophy and keratoses all existed side by side.

Multiple Hæmangiomata.

DR. HOWARD WILLIAMS presented a girl, aged twelve years, who had the very uncommon disorder of multiple angiomata in the skin and other viscera. The main clinical manifestations were recurring angiomata in the skin, recurrent severe anæmia from bleeding intestinal angiomata, and multiple calcified nodules in the liver. The girl came from healthy parents and was the youngest of three children. No other members of the family or relatives had hæmangiomata, nævi or bleeding disorders. She had been a full-term healthy baby and had made normal progress until the age of two years, when a lump developed on the calf of the right leg. Exploratory operation proved this to be a hæmangioma, which had infiltrated the muscle mass of the calf. Surgical removal was not attempted, and X-ray therapy was administered to the leg, after which the lump disappeared. Her health was then good until the age of seven years, when a

swelling developed on the right side of her chest in the region of the outer border of the scapula. This proved to be another hæmangioma, which was removed surgically. Shortly after this, and for the next five years, episodes of anæmia occurred, but at no stage was there any evident blood loss or other cause revealed to account for them. From the ages of seven to nine years iron and liver therapy seemed to produce a spontaneous remission of the attacks of pallor. From nine to eleven years she was very well and had a good colour, but one year before the meeting she had become very pale and the anæmia did not respond to iron and liver therapy, so a transfusion of blood was given. Shortly after this transfusion she became pale and anæmic again, and a further blood transfusion was necessary. Temporary improvement followed, but gradually pallor recurred, and at this stage she was admitted, on June 7, 1950, to the Children's Hospital. Clinical examination showed an intelligent, well-developed, pale girl with a weight of five stone three and a half pounds and a height of four feet nine inches. There was a purplish hæmangioma, one centimetre in diameter, on the plantar surface of the right small toe, and a very small hæmangioma two to three millimetres in diameter on the lateral aspect of the right thigh. Two linear operation scars were present, one on the lateral aspect of the lower part of the right leg and the other on the right side of the chest, immediately behind the posterior axillary fold. The liver and spleen were not palpable, and lymph glands were not enlarged. The following investigations were carried out. Blood examination showed a hæmoglobin value of 40% (5·8 grammes per 100 millilitres) and totals of 3,400,000 red blood cells and 7800 white blood cells per cubic millimetre. The red cells showed some anisocytosis and poikilocytosis, and many of the cells were poorly stained. Reticulocytes numbered 4% and platelets were normal. The response of the serum to the Van den Bergh test was negative, and the fragility of the red cells was normal. Bone marrow biopsy showed a normal hyperactive marrow, and the pathologist considered that the appearance was compatible with a marrow responding to the stimulus of blood loss. The child's stools were normal in appearance, but tests for occult blood yielded a persistently positive result. Sigmoidoscopic examination showed a normal rectum and sigmoid colon. Radiological examination of the alimentary tract on two occasions failed to reveal any lesion in œsophagus, stomach, duodenum, small intestine or colon. X-ray examination of the bony skeleton revealed normal findings, but a number of rounded calcified nodules were seen in the region of the hæmangioma of the right calf which had been treated previously with deep X-ray therapy, and two similar small nodules were seen in the muscle tissue immediately above the left elbow joint. Similar lesions were seen in large numbers and varying in size from several millimetres in diameter up to half a centimetre, scattered throughout the liver and also in the pancreas. The following tests to assess liver function all gave normal results: plasma prothrombin estimation (85%), thymol turbidity test (less than one unit), thymol flocculation test (negative result), serum alkaline phosphatase estimation (5·6 units—King and Armstrong), total serum protein estimation (5·9 grammes per 100 millilitres), serum albumin estimation (3·6 grammes per 100 millilitres) and serum globulin estimation (2·3 grammes per 100 millilitres).

A clinical diagnosis of multiple hæmangiomata with severe anæmia from intestinal bleeding due to angiomata was made, and Dr. J. G. Whitaker undertook abdominal exploration after the child had received a blood transfusion to restore the hæmoglobin level to normal. In the three to four feet of the small intestine below the duodenojejunal flexure, five angiomata of varying size were identified. The most distal one was the apex of a chronic, non-obstructive intussusception, which reduced very easily. This angioma was polypoid in character and could easily be seen as a bluish swelling of approximately half an inch in diameter on the bowel wall. Three other angiomata were of similar size; they seemed to infiltrate the muscle wall and were seen as bluish irregular masses in the bowel wall. One other formed a polypus, which could be felt inside the lumen; it could not be seen through the bowel wall, but could be transilluminated as a dark mass half an inch in diameter. The intestine in between the angiomata was thickened and was more vascular than normal. The thickening appeared to involve the entire bowel wall. Its nature was uncertain, but was in great contrast to the remainder of the small intestine. The liver was not enlarged, but presented a very remarkable sight, the entire upper surface being studded with multiple angiomata, some of which had small nodules of calcium in the centre. No normal liver tissue could be seen. A biopsy specimen was taken and the pathologist, Dr. Alan Williams, made the following report:

> The specimen consisted of three small calcified nodules, with an adherent small mass of soft tissue. Section of the soft tissue revealed large spaces in which red cells are seen. These spaces are lined by single layer of endothelium and the walls consist of dense, fibrous tissue. In some areas, hæmorrhage has apparently occurred, as iron-containing pigment is seen in macrophage cells. Calcium deposition is occurring in places. The appearance is not that of a malignant tumour, but rather that of a vascular, developmental anomaly, or "hamartoma".

The abdomen was closed, as Dr. Whitaker considered that resection of the diseased area was too large an undertaking and local resection was a "hit and miss" measure, as there was no means of determining the site of bleeding. Furthermore, the liver seemed to be the seat of a very gross and extensive lesion.

Dr. Williams said that there seemed to be no doubt about the diagnosis, but the great problem was what should be done for the girl. Should she still be observed and, if she became anæmic again, which was very probable, be treated with hæmatinics and blood transfusion, or should an attempt be made to eradicate the bleeding focus by extensive resection of the diseased gut? As far as could be determined by the methods of visual inspection by transillumination and palpation that was the only area of the alimentary tract that seemed abnormal.

DR. LESLIE HURLEY said that he was in full agreement that the central problem was the future management of the child, although there were many features of very great interest in the girl's illness. The difficulty was that there was no previous clinical experience to guide one as to what was likely to be the natural history of the disease. He thought that almost certainly the cause of the anæmia was blood loss from one or more of the angiomata bleeding into the alimentary tract, but the large number of angiomata in the liver might have upset liver function and thus helped to contribute to the anæmia. The severe attacks of anæmia over the past year made it probable that bleeding was likely to continue, and her life and health be jeopardized. The risk of severe bleeding seemed on the whole to be greater than the risk of removing surgically the diseased bowel.

DR. DOUGLAS STEPHENS, JUNIOR, thought that surgical removal of the diseased part of the bowel was the correct management of the child, and he did not consider the risk as being unduly high.

DR. H. BOYD GRAHAM referred to intracranial calcification in Sturge-Weber disease and thought that there was a close parallel to the calcification in the liver in the child under discussion.

DR. P. CODY said that from the radiological viewpoint the type of calcification in the liver of the child presented was different from that of the intracranial calcification in the Sturge-Weber syndrome. The appearance of the calcified nodules in the girl under discussion was identical with that of phleboliths and was quite different from the spotted calcification in Sturge-Weber disease.

Dr. Howard Williams, in summing up, considered that the major difficulty in deciding whether to advise surgical treatment was that the natural history of the disorder was not clearly known and that any opinion was being given on insufficient evidence. It was possible that thrombosis might occur and the bleeding cease. Surgery was not free from risk, and a guarantee of cure could not be given with certainty, even if it was undertaken. He was inclined to observe the child, and if severe anæmia returned, or any other accident such as an acute intussusception jeopardized her life and health, then the risk of surgery would be justifiable.

Pertussis Hæmagglutinin.

DR. STEPHEN FISHER said that the organism which was generally regarded as the cause of whooping-cough had been described by Bordet and his collaborators in the early years of the present century. The development of prophylactic vaccines had soon followed the discovery, and in 1914 the Council on Pharmacy and Chemistry of the American Medical Association placed pertussis vaccine on its list of "New and Non-official Remedies". However, the preparation was struck off the list in 1931, only to be reintroduced recently. Although Louis Sauer, in a series of papers from the early 1930's, reported good protection in children from use of his vaccines, MacFarlan, Topley and Fisher, in a field trial in England in 1945, found no significant difference in the incidence of pertussis between two groups of children, one of which had been vaccinated and the other not.

These differences of opinion were, of course, due to gross variations in the protective power of the vaccines, and the variations in the vaccines were caused by two factors. Firstly, there was not enough known about the relationship of the immunizing power of the organism to its bacteriological properties, and secondly, it was difficult to assess the immunizing power of a vaccine in the laboratory. It was interesting to note that the early work of Bordet and his colleagues had touched on both of these problems and initiated long lines of research. As regards the bacteriology of the organism, they found that freshly isolated strains contained agglutinogens which were different from those present in laboratory strains accustomed to grow on simple media and no longer requiring the presence of blood. Those findings were confirmed in 1931 by Leslie and Gardner, who described the so-called "phases" of the organisms. Virulent, freshly isolated organisms were in phase 1 and contained an antigen characteristic to that phase, the so-called phase 1 agglutinogen. Most bacteriologists still regarded the phase 1 characteristics as criteria of virulence and as indications of full immunizing potency.

Bordet and his co-workers had noted the paroxysmal cough and the convulsions present in clinical cases and attributed those symptoms to the presence of a toxin. They could find no exotoxin, so they extracted an endotoxin. This material killed mice when it was injected into them by the intraperitoneal route, and the effect could be obtained also if whole live organisms were injected instead. Evans and Maitland found in 1937 that the toxic effects on mice could be neutralized with antiendotoxin prepared in rabbits. In this way a test was developed involving use of the intraperitoneal route of challenge. The role of endotoxin as a protective antigen in pertussis was still a subject of controversy.

In 1937, Burnet and Timmins had reported that mice could be infected with pertussis by instilling a suspension of a fresh culture into the nose of the lightly anæsthetized animal. The intranasal inoculation was followed by the development of specific bronchitis, bronchiolitis and interstitial pneumonia; if the dose was large enough, the animals died. The disease produced in the mouse in this fashion was the nearest experimental approach to the naturally occurring condition in the human subject; furthermore, it could be used to test for immunity, as efficient immunization would prevent or alleviate the effects of the challenging inoculation. However, owing to certain difficulties inherent in the test, it had not gained universal acceptance as part of the procedure for testing the efficiency of vaccines. American workers had therefore developed a new method of challenging immunized animals. This consisted of intracerebral injection of the organisms. The method was in fairly general use in the United States. Nevertheless, the intranasal method of infecting mice had been used successfully, particularly in Australia.

Dr. Fisher then went on to say that investigations on whooping-cough had been commenced at the Commonwealth Serum Laboratories in the late 1930's by a team consisting of Dr. E. V. Keogh, Dr. E. A. North and Mr. G. Anderson, with Dr. S. W. Williams on the clinical side. The inquiry was first directed to find out whether the antigens which were then known, the endotoxin and the phase 1 agglutinogen, played any part in the production of immunity against intranasally introduced experimental pertussis in mice. No immunity was found in the inoculated mice. This conclusion was based, to a large extent, on the finding that the serum from an adult who had been in contact with a patient with pertussis contained a considerable amount of protective antibody against intranasally introduced pertussis, but none against endotoxin and very little against phase 1 agglutinogen.

The next step was a finding by Dr. E. V. Keogh and Dr. E. A. North that virulent pertussis bacilli contained a hæmagglutinin. The hæmagglutinin was present also in the supernatants of cultures which were grown in special broth. The relationship of hæmagglutinin to the experimental disease in the mouse was then investigated. It was found that the virulence of strains to mice, exposed to infection by the intranasal route, depended on their hæmagglutinin content. In protection tests, strains which contained hæmagglutinin conferred immunity, and strains devoid of hæmagglutinin failed to do so. It was found also that hæmagglutinin was a potent antigen, and that in passive protection experiments the potency of a serum was determined by its antihæmagglutinin content. The serum from an adult contact, previously referred to, which had been found to be a powerful protecting agent, although devoid of antiendotoxin and poor in bacterial agglutinin, was now examined for antihæmagglutinin and was found to contain this antibody in high titre. Antihæmagglutinin was present also in the serum of children convalescing from whooping-cough.

Dr. Fisher said that the significant fact of this work was that it was possible to produce in the mouse an experimental disease which closely resembled the human condition, and that an antigenic fraction had been identified which was both virulence factor and essential immunizing antigen for that type of experimental disease. The results suggested that hæmagglutinin might be the essential immunizing antigen in man. This suggestion raised two questions. The first was whether the view of hæmagglutinin as the essential effective antigen in man was compatible with the ideas of most American workers, who believed that the presence in children's serum of a certain titre of bacterial agglutinin (the antibody specific to phase 1 agglutinogen) was the criterion of immunity. These views seemed compatible, because most strains which were rich in phase 1 agglutinogen contained some hæmagglutinin as well. The second question was whether it had been proved that hæmagglutinin was an effective antigen against whooping-cough in man. That question must await the result of a field trial. It was hoped that the trial would be carried out very soon.

The last phase of the work was the purification and stabilization of the antigen. Dr. E. V. Keogh had first succeeded in extracting the hæmagglutinin from the bacterial bodies. It was then found that the hæmagglutinin adsorbed readily to aluminium phosphate floccules, and a detailed process for adsorption and purification was worked out by Mr. M. F. Warburton. The final product was a potent antigen, one millilitre of the preparation containing the antigen extracted from 10,000 to 20,000 million organisms. During the past twelve months a few small-scale clinical trials had been carried out in collaboration with Dr. S. W. Williams and, more recently, with Dr. H. N. B. Wettenhall. The soluble hæmagglutinin had been used first, and then the aluminium phosphate adsorbed antigen. The trials were carried out in order to judge antibody response and to detect any toxic effects. It was found that two doses of the soluble product were required to obtain an appreciable antihæmagglutinin titre. However, a single dose of the adsorbed preparation, provided it was large enough, was capable of provoking a similar rise. So far, one millilitre of the adsorbed antigen had been administered to 18 babies, none of whom had received previous immunization against whooping-cough. Toxic reactions, both local and general, were mild in all these cases. However, moderately severe reactions were seen in two children who had been immunized previously. It seemed probable that a single injection of the aluminium phosphate adsorbed hæmagglutinin would be sufficient, and, so far as could be judged from the very limited experience, a fairly large dose could be given without any significant toxic effects. However, if it was desired to inject a second dose, or a "booster" dose later on, it seemed advisable to make it small, for example, one-tenth of a millilitre. Further clinical tests, designed to determine the optimal conditions for the administration of the product, were being undertaken.

Finally, Dr. Fisher asked what was the use of immune and hyperimmune sera as prophylactic and therapeutic agents in whooping-cough. Opinions, mainly from the United States, varied a good deal on the usefulness of these agents. Unfortunately, the reports seldom gave data from which the antibody content of the serum could be assessed. Because of this, there was no proper way of evaluating and comparing the results. A concentrated pooled rabbit serum had been prepared at the Commonwealth Serum Laboratories; the rabbits had been given a protracted course of injections of supernatant fluid from pertussis cultures. The serum had a high antihæmagglutinin titre and contained other antibodies as well. It had not yet undergone a thorough clinical trial.

DR. E. V. KEOGH said that if animal experiments meant anything, then a suitable antigen had been prepared for use in immunization of children. The antigen should be safe and reliable, but the final test must be a controlled clinical trial.

DR. ROBERT SOUTHBY and DR. A. P. DERHAM both stressed the importance of having a safe and reliable immunizing agent, one that did not cause reactions and one that needed to be administered only once or twice. They considered that this would be a big step forward in clinical practice, as the present method in use in Melbourne required four or five injections spread over a period of four or five weeks.

Correspondence.

LYMPHOSARCOMA INVADING THE HEART: A REPORT OF THREE CASES WITH AUTOPSY FINDINGS.

SIR: In one of the three cases of lymphosarcoma invading the heart reported by Dr. R. B. Pilcher (September 2, 1950), painful swelling of joints appeared ten months before death.

This calls to mind the pulmonary osteo-arthropathy which in several recently reported cases has complicated neoplasms of the lung. In his original description of osteo-arthropathy as a sign of pulmonary suppuration, Marie (1890) wrote of "pseudorheumatism" in addition to clubbed fingers. Craig (1937) described swollen joints in cases of neoplasm; and in the last few years several such cases have been reported. In many the joint changes exactly resembled rheumatoid arthritis, and in some the joints returned to normal soon after removal of the neoplasm.

In Dr. Pilcher's case, perhaps the onset of the arthritis indicated that lung tissue had been invaded by the mediastinal neoplasm.

Yours, etc.,

34 Queen's Road, Melbourne, September 8, 1950. M. KELLY.

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SINUS EPISTAXIS.

SIR: I cannot recollect reading anything of "sinus epistaxis" and the following notes should be worth recording.

This type of epistaxis is often troublesome and it is difficult to control by simple nasal packing and may even be fatal. My attention was first drawn to the features of the condition about 1935. I saw a male patient in the out-patient department of the Brisbane Hospital, aged about forty-three years, with symptoms of acute left maxillary sinusitis. I did an antral lavage in the usual manner and, as there was a little bleeding, decided to keep the patient in hospital. On my next visit four days later the patient was still bleeding and had had blood transfusion. The bleeding could not be controlled by nasal packing. Thinking that I had probably damaged a vessel in the bony naso-antral wall and that the bone prevented its contracting, I decided to open the antrum in the canine fossa and thus be enabled to deal with the vessel. On opening the antrum I found a much thickened and intensely engorged mucosa, which bled freely on the slightest touch. Removal of this membrane, which in these cases strips off very easily, resulted in cessation of the hæmorrhage, the radical operation was completed, and subsequent progress was quite satisfactory.

I have had a series of these severe cases, probably about 12 in all, but not having my own nor hospital records available, except for the last three, must write from memory. Some cases followed minor surgery as related above, but the majority have been spontaneous in origin. Until leaving Brisbane I treated them all, with one exception referred to later, by radical operation on the maxillary antrum concerned, and in every case the condition of the mucosa was similar, and its removal was followed by cessation of the hæmorrhage. I formed the opinion that the condition was due to infection by hæmolytic streptococci and regret that I did not have the examination made to confirm this or otherwise, but they were all rather in the nature of emergency cases.

The exception mentioned above was an elderly female patient, who had already been under treatment by her medical attendant, admitted to hospital and prepared for operation. Unfortunately she died very soon after my arrival, and I had no time for surgery.

I will now briefly describe two of the spontaneous cases which were operated upon. A man, aged seventy, had had nasal packings for epistaxis for about three days and was still bleeding freely when I saw him in hospital. There were several nasal polypi on that side; he declined radical surgery, not without reason; removal of the polypi was followed by suspension of the hæmorrhage. In not many weeks it recurred very severely; he required and received blood transfusion. I then performed a radical operation on the maxillary sinus involved; the same condition of the mucosa as previously described was present. Not only was the after result satisfactory in this case as regards the hæmorrhage, but by a coincidence a chronic kidney condition for which he was receiving treatment cleared up also.

The second operated case which I here describe could well have been fatal. The patient was a woman, aged about thirty years, within six weeks of her confinement. She had very severe spontaneous epistaxis. Ordinary nasal packing was useless; her medical attendant had prevented the "overflow" of blood by means of a tight post-nasal tampon tied very firmly over nasal packing to a large tampon in the anterior naris. This did not actually affect the condition of hæmorrhage. When I saw the patient I removed this packing and blood poured forth. My "superior" knowledge as a specialist availed me nothing in getting better results from nasal packing, and I could only repeat the procedure of her medical attendant, who had really done a very difficult and efficient job. In forty-eight hours the packing was again removed, but the condition was no better. Eventually after five days of this, including also four blood transfusions and ligation of the external carotid artery, the condition was not relieved and the red cell count was just over two million. I decided to do what I should have done earlier. The patient had her fifth transfusion, and I radically operated upon the maxillary antrum. The condition of the mucosa was, of course, as previously described. The result was eminently satisfactory, the hæmorrhage ceased at once, and the baby was born about the expected date without any trouble.

Since leaving Brisbane I have encountered three further cases of this "sinus epistaxis", but, acting on the assumption that the cause was a hæmolytic streptococcus infection, I have treated these three patients with liberal doses of penicillin, of course also trying to efficiently pack the side of the nose concerned, particularly between the middle turbinate bone and the outer wall of the nasal cavity. In each of these cases the hæmorrhage has become negligible within less than twenty-four hours.

In all of this series of cases the hæmorrhage was severe, one being fatal and a second only saved from a fatal termination by appropriate surgery. Possibly some of the others may have had an unhappy ending without this procedure. There must, however, be many cases of "sinus epistaxis" of less severity which recover spontaneously, and the bleeding may come from other of the nasal accessory sinuses. In the severe cases it is practically impossible to see the source of the bleeding; I have once only, after liberal cocainization, observed a stream of blood coming down in the middle meatus from the maxillary ostium. In the minor cases free usage of adrenaline and cocaine does enable one to find the source of the hæmorrhage.

All these cases occur in the chronic "allergic" or catarrhal and congenital type of nasal sinus disease, and, although often difficult to obtain, careful investigation will elucidate significant past and family history. Patients' negative statements are mostly unreliable. To instance these features I shall refer to my last patient. On August 26, 1950, I visited a male patient in hospital, aged thirty-one years, married, with two children. He had had moderately severe right-sided epistaxis for two days. He had had a cold two weeks previously, but stated that he seldom had colds and had no nose trouble before. His admitted past history included German measles, chickenpox and hives. He strongly denied that he had ever had any other complaint. However, the history of hives was sufficient to put one on the right track. His medical attendant had inserted a post-nasal tampon and packed the nose. Although this lessened the flow of blood, it did not stop the hæmorrhage, but from previous experience I decided not to disturb the packing, as it was unlikely that I would do any better myself. I noticed that he had a troublesome cough with purulent sputum, which he claimed was only since his recent cold. Penicillin by injection was immediately instituted, plus the usual morphine and atropine; he had already received "Coagulin Ciba"; by next morning the hæmorrhage was minimal. On August 27, 1950, the tampon and gauze packing were carefully removed. The nasal cavities were cocainized and then the presence of moderate polyposis on both sides was revealed. The nose was then once more packed with acriflavine gauze, particular attention being paid to the right middle meatus. On August 29, 1950, all hæmorrhage had ceased; there was a moderate secondary anæmia present. I then obtained an amended medical history—the cough had been present for many years, it was bronchiec-

tatic in nature, he also was subject to some attacks of "wheezing"; eventually he will say that he has always had "catarrh", "but I did not think you wanted that". Subsequent sinus X ray naturally confirmed the catarrhal or "allergic" condition of the sinus mucosa. This patient will have a lipiodol examination of the lungs, penicillin by inhalation for a full course and some sinus surgery, but as little of that as is necessary. He should also benefit from large doses of vitamins *A* and *D* over an indefinite period.

In conclusion, I wish to stress the fact that, in spite of the patient's denial of past symptoms, painstaking inquiry will eventually elucidate various personal and family symptoms indicating that these sinus conditions are familial and congenital in origin and are only a feature of a basic biochemical dysfunction. Proper treatment demands a recognition of this and cannot be merely regarded as the treatment of a more or less simple local condition.

I wish to stress the further point that although symptoms and examination, including X ray, may only inculpate one or more of the nasal accessory sinuses, it is a case of "one in, all in", that is, the mucosa of all the nasal accessory sinuses is involved to a greater or lesser extent in the morbid process.

Yours, etc.,

ERNEST CULPIN.

Marine Parade,
Labrador,
Southport,
Queensland.

September 6, 1950.

RUBELLA IN PREGNANCY: THE OBSTETRICIAN'S PROBLEM.

SIR: In your issue of September 9 last you report a symposium on rubella. One heading under which this was discussed was "The Obstetrician's Problem".

Surely there is no obstetrical problem but a moral one. If it is claimed that it is justifiable to destroy the unborn child because it may be defective and because this knowledge may affect the mother's health, could not an even better case be made out for the destruction of a spastic idiot, the care of whom was undermining the mother's health, both mental and physical? This, of course, would be straight out murder, but the principle is entirely the same.

In the case of rubella a logician might ask, would it not be more logical to allow the pregnancy to continue and the child to be born? If the child were than found to be defective, it could be destroyed (humanely, of course!), but if it were normal, then it would be allowed to live. This procedure would save the lives of many healthy babies which would otherwise have been unnecessarily sacrificed.

No, the problem of destruction of life, born or unborn, is a moral one, and unless one holds fast to the firm principle that human life is inviolable, abortions will be done for an ever-increasing variety of reasons, social, economic *et cetera*, through a misguided sense of pity and humanitarianism.

Yours, etc.,

FRANCIS J. HAYDEN, F.R.C.O.G., F.R.C.S.

55 Collins Street,
Melbourne,

September 14, 1950.

DEATH CERTIFICATES IN NEW SOUTH WALES.

SIR: In the book of forms supplied to registered medical practitioners, "Registration of Births, Deaths, and Marriages Act, 1899-1934 (Ninth and Eleventh Schedules)", there purports to be, at the foot of each form to be delivered to the District Registrar, a quotation of Section 27A as under:

> By Section 27A of the abovementioned Act, the medical practitioner who has attended any deceased person during his last illness is required to—
>
> (1) sign and deliver or forward forthwith to the District Registrar a certificate in the above form stating the cause of death;
>
> (2) deliver to the tenant of the house or place in which the death occurred a notice in writing in the form herewith, which may be detached for that purpose;
>
> (3) in case of sudden death or where in his opinion death has occurred under any circumstances of suspicion, forthwith report the case to the coroner.
>
> Where the deceased was not attended during his last illness by a legally qualified medical practitioner, a legally qualified medical practitioner who has viewed the body, if satisfied that death was due to natural causes, shall—
>
> (1) sign and deliver or forward a certificate in the above form to the District Registrar;
>
> (2) deliver to the tenant of the house or place where the death occurred a notice in the form herewith, which may be detached for that purpose.

This is not an accurate quotation. "Required to" here replaces "shall" in the Act. After each paragraph (1) and (2) the word "and" has been omitted in the quotation. This means that in the case of (3) the practitioner has to comply with both (1) and (2) as well.

This state of affairs seems to me anomalous, amounting almost to an absurdity. Hitherto the students have been taught in the lectures in medical jurisprudence that when they report to the coroner their duty is done. One has only to imagine under the circumstances there might be suspicion of poisoning, or criminal abortion or any other similar situation, and the practitioner having to commit himself to an opinion to the Registrar in what is an official document.

Further, in the case where the deceased was not attended before death. In this case the teaching has always been not to give a death certificate, but to notify the coroner through the police and if you have a decided opinion to give a note expressing the opinion. The matter is then in the hands of the coroner. He deals with the matter as he thinks fit, either issuing an order or have further investigation made by his officers.

I am writing this in the hope that the attention of the authority who deals with these matters will have the anomalies rectified.

Yours, etc.,

STRATFORD SHELDON,
Lecturer in Medical Jurisprudence,
University of Sydney.

28 O'Connell Street,
Sydney,

September 18, 1950.

LEUCOTOMY AND CHRONIC PSYCHOSIS.

SIR: It is worth while to stop and reflect on the recent report by Dr. Grey L. Ewan to the State Minister of Health upon the advisability of leucotomy in cases of chronic psychosis. This report contained stern and justifiable warnings.

1. Let us remember that the frontal lobe is the latest acquisition of mankind in phylogenetic evolution. It is poorly developed even in higher mammals. Tandler called the species *Homo sapiens* a frontal lobe animal, and the comparative anatomists may agree with him. Is it right to reverse evolution?

2. Can leucotomy (and its modifications) be regarded as rational causal therapy until we are able to exclude the social ætiology of morbid human beheaviour?

Yes, there are some marvellous recoveries from the schizophrenic syndrome after leucotomy. For argument's sake, however, no one would regard splenectomy as a rational cure for malaria today, even though some cases should recover after it. Yet results such as this, in the absence of any other knowledge, could easily make an impression on a student's mind.

Even today many great authorities disagree when they define the term "schizophrenia". Some prefer to use only "schizophrenic reaction", "schizophrenic condition"; others like to avoid the term "schizophrenia" altogether, as long as the community judges the gravity of a particular mental disorder according to the risks or nuisance to the environment caused by the patient. At the same time the therapeutic setbacks of psychoanalytical and neurophysiological approaches to psychosis make it clear that sociology and psychiatry are inseparable, and that there is no better training for the one than a close study of the other.

On the other hand, the frontal lobe is generally considered to be the centre of intelligence, for with its extensive damage the patient loses the more decent habits of civilization. The term "intelligence" (defined as "a peculiar power of the mind to adapt incessantly, and to fight successfully against the environment") overlaps other notions. Intelligence is not a constant condition even in a man of excellent intelligence. It seems that the meaning of the term "intelligence" changes according to the needs and circumstances of the community.

All these reflections may appear to be the reflections of a pedantic bookworm. But the latter is right to demand that (i) research should start on a foundation of clearly defined terms, (ii) it should be directed to the cause of the disease, and (iii) symptomatic therapy should not endanger life.

Wagner-Jauregg once tried to cure the katatonic type of schizophrenia by castration. He had good therapeutic results; when he failed, he attributed it to a third cryptic testicle in the abdomen!

Once I suggested partial liver resection; the liver being the second largest blood reservoir in the body, I hoped to relieve the blood circulation of the cerebrum by such an operation. I hoped that such an experiment would lead to fruitful research concerning the physiological interplay of liver and cerebrum. A number of psychiatrists were scared by the idea, and I can see now that such an experiment would leave the field more involved and confused than ever. After much effort, leucotomy has not advanced the study of cerebral physiology either.

Ewan also emphasizes the risks of broadening the indications for the operation. Let us wonder whether, by these heroic experiments, we do not fall back on the ancient formula: *"Vulnera dum sanas, dolor est medicina doloris."*

Yours, etc.,

235 Macquarie Street,
Sydney,
September 15, 1950.

ALEXANDER FRANK.

Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Week-End Course at Newcastle.

THE Post-Graduate Committee in Medicine in the University of Sydney announces that a week-end course will be held at the Royal Newcastle Hospital, Newcastle, in conjunction with the Central Northern Medical Association, on Saturday and Sunday, October 28 and 29, 1950. The programme will be as follows.

Saturday, October 28: 2 p.m., registration; 2.30 p.m., "Biochemistry in General Practice", Dr. F. S. Hansman; 4 p.m., "Diseases of the Rectum", Dr. T. Edward Wilson.

Sunday, October 29: 10 a.m., "Recent Advances in Therapeutics", Dr. A. W. Morrow; 11.15 a.m., "The Investigation of Renal Function", Dr. F. S. Hansman; 2 p.m., "The Management of Complications following Abdominal Operation", Dr. T. Edward Wilson; 3 p.m., "The Modern Management of Some Renal and Hepatic Diseases", Dr. A. W. Morrow.

The fee for attendance is £2 2s. A fee of £1 is being charged in addition to the course fee to cover entertainment expenses. Those wishing to enrol are requested to communicate without delay to Dr. W. P. McLaughlin, Honorary Secretary, Central Northern Medical Association, 130 Glebe Road, Merewether, Newcastle.

Week-End Course in Electrocardiography.

The Post-Graduate Committee in Medicine in the University of Sydney announces that a week-end course in electrocardiography, suitable for general practitioners, will be held on Saturday and Sunday, November 4 and 5, 1950, in the Maitland Lecture Theatre, Sydney Hospital. The programme is as follows:

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED SEPTEMBER 9, 1950.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.[2]	Western Australia.	Tasmania.	Northern Territory.[3]	Australian Capital Territory.[3]	Australia.[3]
Ankylostomiasis	*	..	2	..	..	..	..	..	2
Anthrax	*	..	..	*	..	..	..	*	..
Beriberi	*	*	*	..	*	*	..	..	..
Bilharziasis	*	..	..	..	..	..	..	..	..
Cerebro-spinal Meningitis	1(1)	3	1	..	..	..	..	..	5
Cholera	..	..	..	*	..	..	*	*	..
Coastal Fever(a)	*	*	..	*	*	*	..	*	..
Dengue	..	..	*	..	*	*	..	..	..
Diarrhœa (Infantile)	..	..	1(1)	..	1(1)	..	..	..	2
Diphtheria	8(1)	3(2)	2(2)	..	2(2)	..	..	..	15
Dysentery (Amœbic)	*	..	..	..	..	..	..	..	..
Dysentery (Bacillary)	*	..	..	..	1(1)	..	..	..	1
Encephalitis Lethargica	..	..	..	..	..	..	..	..	..
Erysipelas	*	*	*	..	*	*	..	..	..
Filariasis	*	..	..	..	..	..	..	..	..
Helminthiasis	*	..	*	*	*	*	*	*	..
Hydatid	*	1	*	*	..	*	*	..	1
Influenza	*	*	*	..	*	*	..	*	..
Lead Poisoning	*	*	1(1)	*	*	*	*	*	1
Leprosy	..	..	..	..	2	..	..	..	2
Malaria(b)	..	..	1(1)	..	1	..	..	..	2
Measles	*	*	*	..	*	*	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	18(12)	1	3(1)	..	1(1)	..	..	..	23
Psittacosis	*	..	*	..	*	*	*	*	..
Puerperal Fever	..	..	1	..	..	..	..	..	1
Rubella(c)	*	*	..	*	1(1)	..	..	..	1
Scarlet Fever	13(9)	22(16)	6(4)	..	3(1)	1	..	..	45
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	*	..	2	*	*	*	*	*	2
Trachoma	*	..	*	*	*	*	*	*	..
Tuberculosis(d)	32(18)	11(6)	15(5)	..	2(1)	5(2)	..	..	65
Typhoid Fever(e)	..	..	1	..	..	..	..	..	1
Typhus (Endemic)(f)	1	..	..	..	1(1)	..	..	..	2
Undulant Fever	..	..	..	..	1	..	..	..	1
Weil's Disease(g)	*	*	1	*	*	*	*	*	1
Whooping Cough	*	*	*	..	*	*	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] The form of this table is taken from the *Official Year Book of the Commonwealth of Australia*, Number 37, 1946–1947. Figures in parentheses are those for the metropolitan area.
[2] Figures not available.
[3] Figures incomplete owing to absence of returns from the Northern Territory, South Australia and Australian Capital Territory.
* Not notifiable.
(a) Includes Mossman and Sarina fevers. (b) Mainly relapses among servicemen infected overseas. (c) Notifiable disease in Queensland in females aged over fourteen years. (d) Includes all forms. (e) Includes enteric fever, paratyphoid fevers and other Salmonella infections. (f) Includes scrub, murine and tick typhus. (g) Includes leptospiroses, Weil's and para-Weil's disease.

Saturday, November 4: 2 p.m., "Abnormal Auricular and Ventricular Rhythms", Dr. W. E. Fisher; 3 p.m., "Heart Block and Bundle Branch Block", Dr. Frank L. Ritchie.

Sunday, November 5: 10 a.m., "Coronary Artery Insufficiency and Cardiac Hypertrophy", Dr. Justin Markell; 11 a.m., "Myocardial Infarction and Similar Electrocardiographic Pictures", Dr. John H. Halliday; 12 noon, question time.

Candidates are asked to submit specific questions in writing to be received at the office not later than October 25, 1950, when arrangements will be made for the particular lecturers to be present at the question time session.

The fee for attendance is £1 1s., the closing date for receipt of applications being October 27, 1950. Those wishing to enrol are requested to forward remittance to the Course Secretary, the Post-Graduate Committee in Medicine, 131 Macquarie Street, Sydney, as soon as possible. Telephones: BU 5238, BW 7483.

Week-End Course in Endocrinology.

A week-end course in endocrinology, suitable for general practitioners, will be conducted on Saturday and Sunday, November 11 and 12, 1950, the programme being as follows:

Saturday, November 11, in the Maitland Lecture Theatre, Sydney Hospital: 2 p.m., "Pituitary Disease: Pituitary Hyperfunction and Pituitary Interrelationships", Dr. Scott Charlton; 2.45 p.m., "Pituitary Hypofunction and Simmond's Syndrome", Dr. James Isbister; 3.30 p.m., "Hyperthyreoidism", Dr. Francis Rundle; 4.15 p.m., "Myxœdema", Dr. E. H. Stokes.

Sunday, November 12, in the A2 Lecture Theatre, Royal Prince Alfred Hospital, Camperdown: 9.30 a.m., "Addison's Disease", Dr. Keith S. Harrison; 10.30 a.m., "Adrenal Hyperactivity: Adrenogenital Syndrome and Cushing's Syndrome", Dr. C. W. G. Lee; 11.30 a.m., "Gonadal Dysfunction in the Female", Dr. F. A. Maguire; 2 p.m., "Hypogonadism", Dr. John Cobley; 2.45 p.m., "Biochemical Investigations in Endocrine Disorders", Dr. E. M. A. Day.

The fee for attendance is £2 2s., and the closing date for receipt of applications is November 3, 1950. Application, enclosing remittance, should be forwarded to the Course Secretary, the Post-Graduate Committee in Medicine, 131 Macquarie Street, Sydney, at an early date. Telephones: BU 5238, BW 7483. Telegraphic address: "Postgrad Sydney."

Congresses.

THE INTERNATIONAL CONGRESS OF RADIOLOGY.

THE Sixth International Congress of Radiology was held at London in July, 1950. At a reception on July 25, 1950, at the Royal College of Surgeons, Lincoln's Inn Fields, Honorary Fellowships of the Faculty of Radiologists were conferred upon: Professor G. Forssell, Sweden; Professor H. R. Schinz, Switzerland; Dr. A. C. Christie, United States of America; Dr. George Pfahler, United States of America; Professor W. A. Jones, Canada; Dr. A. T. Nisbet, Sydney, Australia; Professor S. F. Oosthuizen, South Africa; Sir Stanford Cade, Great Britain. Our congratulations are offered to Dr. Nisbet.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Flood, Martin Joseph, M.B., B.S., 1950 (Univ. Sydney), 42 Wilga Street, Concord West.

Wilson, Lionel Leopold, M.B., 1950 (Univ. Sydney), Balmain Hospital, Balmain.

The undermentioned have been elected as members of the New South Wales Branch of the British Medical Association:

Frank, Chana-Halina, registered in accordance with the provisions of Section 17 (1) (*c*) of the *Medical Practitioners Act*, 1938-1945, 25 Bayswater Road, King's Cross.

Gries, Leon, registered in accordance with the provisions of Section 17 (1) (*c*) of the *Medical Practitioners Act*, 1938-1945, 17 Knox Street, Double Bay.

Markus, John George, M.B., B.S., 1950 (Univ. Sydney), Royal North Shore Hospital, St. Leonards.

Morgan, Edward Hunter, M.B., B.S., 1950 (Univ. Sydney), St. George Hospital, Kogarah.

O'Sullivan, Eibhlin Maire Eilis, M.B., B.S., 1950 (Univ. Sydney), 13 Black Street, Vaucluse.

Shand, William Neil, M.B., Ch.B., 1944 (Univ. Glasgow), 49 Church Street, Randwick.

Torpy, Denys Clifton, M.B., B.S., 1948 (Univ. Sydney), Department of Biochemistry, University of Sydney, Sydney.

Diary for the Month.

OCT. 3.—New South Wales Branch, B.M.A.: Council Quarterly.
OCT. 4.—Victorian Branch, B.M.A.: Branch Meeting.
OCT. 4.—Western Australian Branch, B.M.A.: Council Meeting.
OCT. 5.—South Australian Branch, B.M.A.: Council Meeting.
OCT. 6.—Queensland Branch, B.M.A.: Branch Meeting.
OCT. 10.—New South Wales Branch, B.M.A.: Executive and Finance Committee; Organization and Science Committee.
OCT. 13.—Queensland Branch, B.M.A.: Council Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney)—All contract practice appointments in New South Wales.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federal Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178 North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

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